FILE 'USPAT' ENTERED AT 14:35:24 ON 29 JUN 95

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E              *  *      U.S. PATENT TEXT FILE                    *  * * * * * * * * * * * *
* * * * * * * * * * * * * * * * * *

= > s colloid?(w)gold
      45337 COLLOID?
      49599 GOLD
L1      271 COLLOID?(W)GOLD

= > s l1 and interleukin
       1835 INTERLEUKIN
L2        5 L1 AND INTERLEUKIN

= > d l2 1-5 cit
```

1. 5,292,642, Mar. 8, 1994, Methods and compositions for the detection of monocyte cytotoxicity inducing factor; C. Michael Jones, 435/7.24, 7.92, 810; 436/64, 548; 530/351, 388.23, 389.2 [IMAGE AVAILABLE]
2. 5,286,482, Feb. 15, 1994, Methods and compositions for inducing monocyte cytotoxicity; C. Michael Jones, 424/85.1, 85.2; 514/2, 8, 21 [IMAGE AVAILABLE]

3. 5,262,319, Nov. 16, 1993, Method for obtaining bone marrow free of tumor cells using transforming growth factor .beta.3; Kenneth K. Iwata, et al., 435/240.2, 240.25; 530/399 [IMAGE AVAILABLE]

4. 5,213,804, May 25, 1993, Solid tumor treatment method and composition; Francis J. Martin, et al., 424/450, 78.31, 426 [IMAGE AVAILABLE]

5. 5,112,948, May 12, 1992, Methods and compositions for inducing monocyte cytotoxicity; C. Michael Jones, 530/351; 424/85.1, 85.2; 514/2, 8, 21; 530/350, 827 [IMAGE AVAILABLE]

```
= > d l2 1-5 cit kwic


= > s colloid?(w)metal
      45337 COLLOID?
     663644 METAL

L3      409 COLLOID?(W)METAL

= > s l3 and interleukin
       1835 INTERLEUKIN
L4        3 L3 AND INTERLEUKIN

= > d l4 1-4
```

1. 5,401,767, Mar. 28, 1995, Compounds which inhibit complement and/or suppress immune activity; Robert D. Sindelar, et al., 514/462, 468, 470, 615, 885; 549/345 [IMAGE AVAILABLE]

2. 5,366,986, Nov. 22, 1994, Compounds which inhibit complement and/or suppress immune activity; Robert D. Sindelar, et al., 514/374, 382, 462; 548/237, 252; 549/236, 264, 345 [IMAGE AVAILABLE]

3. 5,173,499, Dec. 22, 1992, Compounds which inhibit complement and/or suppress immune activity; Robert D. Sindelar, et al., 514/462, 825; 549/345 [IMAGE AVAILABLE]

=> d l4 1 kwic

US PAT NO: 5,401,767 [IMAGE AVAILABLE] L4: 1 of 3
SUMMARY:

BSUM(61)
6.37.3. Demonstration of Inhibition of Cell Surface Interleukin -2 Receptor Expression

DRAWING DESC:

DRWD(7)

FIG. 6 demonstrates the inhibition of interleukin -2 receptor (IL-2R) release from PBL by compound 11a. The level of IL-2R in the supernatant of PBL cultures stimulated with. . .

DETDESC:

DETD(48)

Any . . . inhibition of natural killer lysis of target cells, inhibition of proliferation of peripheral blood lymphocytes, or inhibition of cell surface interleukin -2 receptor expression. Specific embodiments of assay procedures which can be used are detailed in the examples sections infra (See Subsections. . .

DETDESC:

DETD(102)

The . . . were carefully added until no more hydrogen was evolved. Cold aqueous 6N hydrochloric acid was then added to dissolve any colloidal metal salts. The resulting product mixture was extracted with ether (4.times.50 ml), dried, and concentrated in vacuo. The residual solid was. . .

DETDESC:

DETD(157)

The . . . inhibition of natural killer (NK) activity, the inhibition of peripheral blood lymphocyte (PBL) proliferation, and the inhibition of cell surface interleukin -2-receptor expression as described infra. In addition, the ability of compound 11a to inhibit the proliferation of Chinese hamster ovary (CHO). . .

DETDESC:

DETD(172)

Release of cell surface interleukin -2-receptor (IL-2R) or CD8 antigen from lymphocytes is a correlate of T cell activation (Rubin et al. J. Immunol. 1985, 135,. . .

DETDESC:

DETD(173)

6.37.3. Demonstration of Inhibition of Cell Surface Interleukin -2 Receptor Expressions

DETDESC:

DETD(174)

The interleukin -2-receptor (IL-2R) is not detectable on the surface of resting T cells. Upon activation by specific antigens or mitogens, T cell proliferation is mediated by an autocrine mechanism whereby activated cells secrete interleukin -2-and express cell surface IL-2R (Meuer, S. C. et al. Proc. Natl. Acad. Sci. U.S.A. 1984, 81, 1509;Tsudo, M., et al.. . .

=> s (colloid?(w)gold(p)toxic?)
45337 COLLOID?
49599 GOLD
85323 TOXIC?
L5 5 (COLLOID?(W)GOLD(P)TOXIC?)

=> d l5 1-5 kwic

US PAT NO: 5,387,676 [IMAGE AVAILABLE] L5: 1 of 5
SUMMARY:

BSUM(22)

The . . . quantitating MN antigen in, for example, clinical samples; as probes for immunoblotting to detect MN antigen; in immunoelectron microscopy with colloid gold beads for localization of MN proteins and/or polypeptides in cells; and in genetic engineering for cloning the MN gene or. . . locate metastases by scintigraphy. Further such antibodies may be used in vivo therapeutically to treat cancer patients with or without toxic and/or cytostatic agents attached thereto. Further, such antibodies can be used in vivo to detect the presence of neoplastic and/or. . .

US PAT NO: 5,368,707 [IMAGE AVAILABLE] L5: 2 of 5
SUMMARY:

BSUM(18)

The . . . those employing the disclosed biosensors, may be used to detect lead as well as a wide variety of nontoxic and toxic metal ions including mercury, cadmium, silver, zinc, copper, calcium, manganese, thallium, etc. However, sensitivity and selectivity of the biosensor will. . . the micromolar or lower ranges of metal ion concentration. Mercury ion, for example, is detected in the nanomolar range employing colloidal gold adsorbed alcohol dehydrogenase biosensors. Lead ion may be quantitatively determined employing immobilized isocitrate dehydrogenase.

US PAT NO: 5,217,594 [IMAGE AVAILABLE] L5: 3 of 5
SUMMARY:

BSUM(17)

The . . . foregoing problems in providing a simple, reliable method of detecting metals in fluids, particularly the detection of trace amounts of toxic metals such as lead and mercury as well as other metals. The method is based on a novel bioelectrode employing colloidal gold adsorbed enzymes that are inhibited, often irreversibly and frequently at submicromolar concentrations of metal ion. Biosensors constructed from such novel. . .

SUMMARY:

BSUM(19)

Biosensors of the invention may be used to detect a wide variety of nontoxic and toxic metal ions including mercury, cadmium, silver, zinc, copper, calcium, manganese, thallium, lead and the like. Sensitivity and selectivity of the. . . metal ion. In most situations, inhibition is preferable in the micromolar or even lower range. In a most preferred embodiment, colloidal gold immobilized isocitrate dehydrogenase may be used to detect submicromolar to nanomolar concentrations of lead ion. Yet another embodiment is a colloidal gold adsorbed alcohol dehydrogenase sensitive to low concentrations of mercury ion.

US PAT NO: 4,487,780 [IMAGE AVAILABLE] L5: 4 of 5
DETDESC:

DETD(8)

As . . . be effective in the treatment of RA, examples of such gold compounds being gold sodium thiomalate, aurothioglucose and ionic gold. Colloidal gold can also be used. Combinations of gold from the above sources with sulfhydryls as listed above present advantages with respect to effectiveness in the treatment of RA and decrease in toxicity . The combination with penicillamine is particularly noteworthy, a principal advantage provided by this combination being the enhanced therapeutic efficacy in. . . to any of the aforenoted substituted cysteines as well as to penicillamine and to cysteine itself. The diminished incidence of toxicity from the combination of gold with penicillamine in comparison to gold alone, is consistent with the fact that penicillamine is effective in the treatment of gold toxicosis in man.

US PAT NO: 4,315,028 [IMAGE AVAILABLE] L5: 5 of 5
DETDESC:

DETD(9)

As . . . be effective in the treatment of RA, examples of such gold compound being gold sodium thiomalate, aurothioglucose and ionic gold. Colloidal gold can also be used. Combinations of gold from the above sources with sulfhydryls as listed above present advantages with respect to effectiveness in the treatment of RA and decrease in toxicity . The combination with penicillamine is particularly noteworthy, a principal advantage provided by this combination being the enhanced therapeutic efficacy in. . . to any of the aforenoted substituted cysteines as well as to penicillamine and to cysteine itself. The diminished incidence of toxicity from the combination of gold with penicillamine in comparison to gold alone, is consistent with the fact that penicillamine is effective in the treatment of gold toxicosis in man.

=> d l5 1-5 cit

1. 5,387,676, Feb. 7, 1995, MN gene and protein; Jan Zavada, et al., 536/23.5; 435/69.1, 240.2, 240.4, 252.3, 254.11, 254.2, 320.1; 536/24.31 [IMAGE AVAILABLE]

2. 5,368,707, Nov. 29, 1994, Convenient determination of trace lead in whole blood and other fluids; Robert W. Henkens, et al., 204/153.12, 153.1, 403; 436/74, 77 [IMAGE AVAILABLE]

3. 5,217,594, Jun. 8, 1993, Convenient determination of trace lead in whole blood and other fluids; Robert W. Henkens, et al., 204/403, 412, 415, 435; 435/288, 817 [IMAGE AVAILABLE]

4. 4,487,780, Dec. 11, 1984, Method of treatment of rheumatoid arthritis; Israel H. Scheinberg, 514/562, 825 [IMAGE AVAILABLE]
5. 4,315,028, Feb. 9, 1982, Method of treatment of rheumatoid arthritis; Israel H. Scheinberg, 514/495, 499 [IMAGE AVAILABLE]

=> d l5 4 cit ab

4. 4,487,780, Dec. 11, 1984, Method of treatment of rheumatoid arthritis; Israel H. Scheinberg, 514/562, 825

[IMAGE AVAILABLE]
US PAT NO: 4,487,780 [IMAGE AVAILABLE] L5: 4 of 5
ABSTRACT:
Rheumatoid arthritis is treated with substituted cysteine compounds having a lower toxicity-to-effectiveness ratio than penicillamine. Such compounds are specific alpha-substituted cysteines, beta-monosubstituted cysteines, beta-di-substituted cysteines other than penicillamine, N-acetyl penicillamine and the N-acetyl derivatives of the alpha and beta-substituted compounds mentioned above.
Any of the compounds may be used synergistically in combination with suitable copper compounds or with suitable gold compounds in the treatment of arthritis.
The same compounds are effective in the treatment of cystinuria and heavy metal poisoning. The same compounds as well as penicillamine are effective in combination with copper in the treatment of heavy metal poisoning.

=> logoff hold
SESSION WILL BE HELD FOR 30 MINUTES
U.S. Patent & Trademark Office SESSION SUSPENDED AT 14:41:35 ON 29 JUN 95
NO CARRIER

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-1995/Aug W3
       (c) format only 1995 Knight-Ridder Info
  File   5:BIOSIS PREVIEWS(R)  1969-1995/Jun W4
       (c) 1995 BIOSIS
  File  73:EMBASE  1974-1995/Iss 24
       (c) 1995 Elsevier Science B.V.

     Set  Items  Description
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?s interleukin(w)2 or il(w)2 or il2

Processing
Processing
Processing
        163764  INTERLEUKIN
       4361744  2
         75725  INTERLEUKIN(W)2
        125883  IL
       4361744  2
         44309  IL(W)2
          4068  IL2
     S1   85401  INTERLEUKIN(W)2 OR IL(W)2 OR IL2
?s s1 and toxic?

         85401  S1
        982091  TOXIC?
     S2    5529  S1 AND TOXIC?
?s s2 and antibod?

          5529  S2
       1114734  ANTIBOD?
     S3    1392  S2 AND ANTIBOD?
?s s1 and toxic?/ti

         85401  S1
        161830  TOXIC?/TI
     S4     627  S1 AND TOXIC?/TI
?s s4 and antibod?/ti

           627  S4
        317095  ANTIBOD?/TI
     S5      19  S4 AND ANTIBOD?/TI
?rd

...completed examining records
     S6      15  RD (unique items)
?t s6/6/1-15


?t s6/7/1-4
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6/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06928284 89230284

Nature of the bifunctional chelating agent used for radioimmunotherapy with yttrium-90 monoclonal ***antibodies*** : critical factors in determining in vivo survival and organ ***toxicity***.

Kozak RW; Raubitschek A; Mirzadeh S; Brechbiel MW; Junghaus R; Gansow OA; Waldmann TA
Division of Cytokine Biology, Center for Biologics Evaluation and Research, FDA, Bethesda, Maryland.

Cancer Res (UNITED STATES) May 15 1989, 49 (10) p2639-44, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: JOURNAL ARTICLE

One factor that is critical to the potential effectiveness of radioimmunotherapy is the design of radiometal-chelated antibodies that will be stable in vivo. Stability in vivo depends on the condition that both the chelate linkage and radiolabeling procedures not alter antibody specificity and biodistribution. In addition, synthesis and selection of the chelating agent is critical for each radiometal in order to prevent inappropriate release of the radiometal in vivo. In the present study, we compare the in vivo stability of seven radioimmunoconjugates that use different polyaminocarboxylate chelating agents to complex yttrium-88 to the mouse anti-human ***interleukin***-***2*** receptor monoclonal antibody, anti-Tac. Chelate linkage and radiolabeling procedures did not alter the immunospecificity of anti-Tac. In order to assess whether yttrium was inappropriately released from the chelate-coupled antibody in vivo, iodine-131-labeled and yttrium-88 chelate-coupled antibodies were simultaneously administered to the same animals to correlate the decline in yttrium and radioiodinated antibody activity. The four stable yttrium-88 chelate-coupled antibodies studied displayed similar iodine-131 and yttrium-88 activity, indicating minimal elution of yttrium-88 from the complex. In contrast, the unstable yttrium-88 chelate-coupled antibodies had serum yttrium-88 activities that declined much more rapidly than their iodine-131 activities, suggesting loss of the radiolabel yttrium-88 from the chelate. Furthermore, high rates of yttrium-88 elution correlated with deposition in bone. Four chelating agents emerged as promising immunotherapeutic reagents: isothiocyanate benzyl DTPA and its derivatives 1B3M, MX, and 1M3B. All four isothiocyanate agents showed prolonged yttrium-88 vascular survival which was essentially identical to that of their iodine-131 activity with only minimum accumulation (1.4-1.8%/g) of the yttrium-88 injected dose into bone. Thus, these four chelating agents were very stable in vivo and suitable for yttrium-monoclonal antibody radioimmunotherapy.

6/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06778480 89080480

Toxicity and therapeutic efficacy of high-dose ***interleukin*** ***2***. In vivo infusion of ***antibody*** to NK-1.1 attenuates ***toxicity*** without compromising efficacy against murine leukemia.

Peace DJ; Cheever MA
Department of Medicine, University of Washington, Seattle 98195. J Exp Med (UNITED STATES) Jan 1 1989, 169 (1) p161-73, ISSN 0022-1007 Journal Code: I2V
Contract/Grant No.: CA-43081; CA-30558; CA-33084; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE

In the current study we used the therapy of established murine leukemia to identify the lymphocyte subsets responsible for toxicity and for therapeutic efficacy of high-dose ***IL***-***2*** . Initial results confirmed that high-dose ***IL***-***2*** induces marked proliferation of a variety of host cells, including NK cells, Lyt-2+ T cells, L3T4+ T cells, and B cells. Infusion of antibody to NK-1.1 depleted NK-1.1+ cells in vivo and greatly reduced the toxicity of ***IL***-***2***, but did not decrease therapeutic

efficacy. By marked contrast, depletion of host T cells, either Lyt-2+ or L3T4+, had no effect on toxicity but greatly reduced therapeutic efficacy. The requirement for host T cells for the curative effect of ***IL***-***2*** gives credence to the possibility that substantial efficacy of high-dose ***IL***-***2*** against established malignancy may require existent host antitumor immunity. Since the human tumors that have been shown to have the most substantial responses to ***IL***-***2*** (i.e., malignant melanoma and renal cell carcinoma) are those long considered to be immunogenic in the autochthonous host, the current study predicts that for these, as well as other immunogenic human tumors, it should be possible to decrease the toxicity and thus increase the therapeutic index of ***IL***-***2*** by selectively depleting NK cells in vivo.

6/7/3 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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10229283 BIOSIS Number: 45029283
ANTI-CD3 ANTI-***IL2*** RECEPTOR CD3 25 BISPECIFIC MONOCLONAL ***ANTIBODY*** BSMAB PROLONGATION OF CARDIAC ALLOGRAFT SURVIVAL WITH LOWER ***TOXICITY*** THAN ANTI-CD3 MAB
WONG J T; WECHER H; MACLEAN J A; SU Z; COLVIN R B; AUCHINCLOSS H MASS. GENERAL HOSP., HARVARD MED. SCH., BOSTON, MA 02090, USA. JOINT MEETING OF THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS AND THE CLINICAL IMMUNOLOGY SOCIETY, DENVER, COLORADO, USA, MAY 21-25, 1993. J IMMUNOL 150 (8 PART 2). 1993. 249A. CODEN: JOIMA
Language: ENGLISH

6/7/4 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1995 BIOSIS. All rts. reserv.

10228935 BIOSIS Number: 45028935
ANTI-CD3 ANTI-***IL***-***2*** RECEPTOR CD3 25 BISPECIFIC MONOCLONAL ***ANTIBODY*** BSMAB T CELL IMMUNOMODULATION WITH REDUCED ACTIVATION AND ***TOXICITY*** THAN ANTI-CD3 MAB IN-VIVO
MACLEAN J A; SU Z; COLVIN R B; WONG J T
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MA 02114, USA.
JOINT MEETING OF THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS AND THE CLINICAL IMMUNOLOGY SOCIETY, DENVER, COLORADO, USA, MAY 21-25, 1993. J IMMUNOL 150 (8 PART 2). 1993. 189A. CODEN: JOIMA
Language: ENGLISH
?s interleukin(w)2 or il(w)2 or il2/ti

Processing
Processing
163764 INTERLEUKIN
4361744 2
75725 INTERLEUKIN(W)2
125883 IL
4361744 2
44309 IL(W)2
947 IL2/TI
S7 84894 INTERLEUKIN(W)2 OR IL(W)2 OR IL2/TI
?s s7 and toxic?/ti

```
        84894  S7
       161830  TOXIC?/TI
    S8    623  S7 AND TOXIC?/TI
?s s8 and antibod?/ti

          623  S8
       317095  ANTIBOD?/TI
    S9     19  S8 AND ANTIBOD?/TI
?rd

...completed examining records
   S10     15  RD (unique items)
?t s10/6/1-15



Set     Items   Description
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S2       5529   S1 AND TOXIC?
S3       1392   S2 AND ANTIBOD?
S4        627   S1 AND TOXIC?/TI
S5         19   S4 AND ANTIBOD?/TI
S6         15   RD (unique items)
S7      84894   INTERLEUKIN(W)2 OR IL(W)2 OR IL2/TI
S8        623   S7 AND TOXIC?/TI
S9         19   S8 AND ANTIBOD?/TI
S10        15   RD (unique items)
?s s1 and colloid?

        85401  S1
        40116  COLLOID?
   S11     53  S1 AND COLLOID?
?rd

...examined 50 records  (50)
...completed examining records
   S12     28  RD (unique items)
?t s12/6/1-28


?t s12/7/4,17,23,25,26,27,28


 12/7/4     (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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08568348   93278348
  Immunotherapy with ***interleukin*** ***2*** after ABMT in AML.  Hamon MD; Prentice HG; Gottlieb DJ; Macdonald ID; Cunningham JM; Smith OP ; Gilmore M; Gandhi L; Collis C
  Department of Haematology,  Royal Free Hospital and School of Medicine, London, UK.
  Bone Marrow Transplant (ENGLAND)  May 1993,  11 (5) p399-401, ISSN 0268-3369  Journal Code: BON
  Languages: ENGLISH
```

Document type: JOURNAL ARTICLE

Myeloablative chemo (+/- radio) therapy and rescue with ABMT has been used as final consolidation therapy in 18 patients with AML in first remission. In seven (6 autologous, 1 syngeneic) marrow reinfusion was followed by iv ***IL***-***2***. One patient, who commenced ***IL***- ***2*** 4 days after BMT, died from pulmonary oedema due to the capillary leak syndrome. Thereafter, treatment with ***IL***-***2*** was delayed until the platelet count reached 30 x 10(9)/l. All patients developed reversible hypotension (treated with infusion of ***colloid***), but treatment was otherwise well tolerated. With 21-58 months (median 32 months) from the time of ABMT there has been one relapse (actuarial risk 17%, 95% confidence intervals (CI) 3-31%). The disease-free survival is 71% (95% CI 38-100%). Eleven patients with comparable remission induction and consolidation therapy, and an identical interval between diagnosis and ABMT (5-11 months, median 6 months) received an autograft without immunotherapy. With 24-45 months (median 29 months) follow-up the actuarial disease-free survival is 36% (95% CI 8-64%), the actuarial relapse risk is 54% (95% CI 18-90%). We conclude that immunotherapy given after ABMT to patients with AML in first remission when the platelet count exceeds 30 x 10(9)/l is safe and may induce an immunological environment which results in the elimination of residual leukaemia.

12/7/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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05011123 83244123

Autoimmune diatheses and T lymphocyte immunoincompetences in BB rats. Maclaren NK; Elder ME; Robbins VW; Riley WJ

Metabolism (UNITED STATES) Jul 1983, 32 (7 Suppl 1) p92-6, ISSN 0026-0495 Journal Code: MUM

Languages: ENGLISH

Document type: JOURNAL ARTICLE

BB rats were found to have autoantibodies to gastric parietal cells, thyroid ***colloid*** antigens, smooth muscle, and thymocytes. No autoantibodies reactive with pancreatic islet cells (cytoplasmic), thyroid epithelial cells, adrenal cortex, testes, or anterior pituitary sections were identified. BB rats with gastric parietal autoantibodies had modest degrees of lymphocytic gastritis, but none developed iron or vitamin B12 deficiencies. These results suggest that BB rats have an underlying autoimmune diathesis. In addition, reports of peripheral T lymphopenia in such rats were confirmed, and markedly reduced helper T cell and cytotoxic-suppressor T cell subsets were demonstrated. Histological studies also revealed depletions of the T cell areas of spleen and lymph nodes. Furthermore, BB rats exhibited a profound inability to reject skin grafts across major and minor histocompatibility barriers. This was confirmed by mixed lymphocyte culture studies in vitro. BB-rat lymphocytes from either spleen or peripheral blood also showed profoundly reduced responses to T cell mitogens. Although BB-rat lymphocytes could produce normal levels of ***interleukin***-***2*** , they were unable to respond to this T cell growth factor. However, examination of thymuses from BB rats showed largely normal histologies, normal numbers of thymocyte subsets, and good mitogenic responses to con A. Thus, it appears that BB rats may have a thymic or post thymic defect in T lymphocyte maturation. The relevance of the immunologic lesion to the etiology of IDD in BB rats remains to be shown.

12/7/23 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
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9344695 EMBASE No: 94290499

Diagnosis and management of acute lung injury

Marinelli W.A.; Ingbar D.H.

Div. of Pulmonary/Critical Care Med., Hennepin County Medical Center, 701 Park Avenue, Minneapolis, MN 55415 USA

CLIN. CHEST MED. (USA) , 1994, 15/3 (517-466) CODEN: CCHMD ISSN: 0272-5231
LANGUAGES: English SUMMARY LANGUAGES: English

Severe acute lung injury, also known as the adult respiratory distress syndrome (ARDS), is a dynamic and explosive clinical syndrome which exacts a mortality of approximately 50%. The criteria for the diagnosis of severe acute lung injury include five principal elements: hypoxemia despite high concentrations of supplemental oxygen, diffuse pulmonary infiltrates on chest radiographs, decreased lung compliance, appropriate antecedent history, and the absence of congestive heart failure. Identifying an appropriate antecedent history requires consideration of a diverse group of etiologies which may injure alveolar structures via either the air-lung or blood-lung interface. The management of patients with acute lung injury should be approached with four principal goals: (1) cardiopulmonary resuscitation and stabilization; (2) rapid identification and elimination of the cause of lung injury; (3) achieving adequate tissue oxygen delivery and support of other end-organs; and (4) prevention, recognition, and aggressive treatment of any complications that develop during the course of therapy. Recent observations have suggested that conventional methods of positive-pressure ventilation may indirectly injure alveolar tissue, thereby perpetuating lung injury. Furthermore, the optimal use of fluid and hemodynamic support remains controversial. Thus, controlled clinical trials are necessary to develop oxygenation, ventilatory, and hemodynamic support strategies which optimize recovery and minimize further injury and to define the role of newer pharmacologic agents in the prevention and treatment of acute lung injury.

12/7/25 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE
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9131063 EMBASE No: 94072171

Biologic and clinical effects of continuous infusion ***interleukin***- ***2*** in patients with non-small cell lung cancer

Ardizzoni A.; Bonavia M.; Viale M.; Baldini E.; Mereu C.; Verna A.; Ferrini S.; Cinquegrana A.; Molinari S.; Mariani G.L.; Roest G.J.; Sharenberg J.; Palmer P.A.; Rosso R.; Ropolo F.; Raso C.
Department of Medical Oncology, Isto. Nazionale Ricerca sul Cancro, Viale Benedetto XV, 10, 16132 Genova Italy

CANCER (USA) , 1994, 73/5 (1353-1360) CODEN: CANCA ISSN: 0008-543X LANGUAGES: English SUMMARY LANGUAGES: English

Background. ***Interleukin***-***2*** (***IL***-***2***) has shown antitumor activity in some neoplasms, such as melanoma and renal carcinoma, but toxicity derived from bolus administration is significant, particularly at the cardiorespiratory level. Methods. To test feasibility, antitumor activity, pulmonary and systemic immunologic effects, and pulmonary function changes of continuous- infusion recombinant ***IL***-***2*** given to patients with non-small cell lung cancer, eleven subjects with Stage III-IV disease were treated in a standard pulmonary medicine unit with a dose of 18 million IU/m2/day from day 1 to day 13 with 1-day rest on day 7. A second induction course was given after a 3-week rest. In patients with nonprogressive disease, four maintenance courses of 6 days' duration at the same dose were planned. Immunologic tests, including lymphocyte phenotype analysis and assays for the detection of tumor necrosis factor (TNF) and of anti-***IL***-***2*** antibodies, were performed before and after treatment in serum and bronchoalveolar lavage fluid (BAL). Cardiopulmonary function tests, including spirometry, arterial blood gas analysis, diffusion capacity, and echocardiography, were obtained before, during, and after treatment. Results. Twenty-one cycles (15 induction courses plus 6 maintenance courses) were administered. No patient was able to complete the six planned courses, and only 3 patients entered the maintenance phase. Reasons for discontinuation included progressive disease in five cases, toxicity in three cases, and patient request in three cases. The most common side effects were fever, hypotension, oliguria, and elevated serum creatinine and liver enzyme levels. No patient required intubation or intensive care. No objective response was seen, and the median survival time was 10 months. Lymphocytosis and eosinophilia were observed in all patients. Surface marker analysis revealed a statistically significant increase in the percentage of CD3+, CD4+, CD25+ and DR+ cells in peripheral blood. Lymphoid cells derived from BAL disclosed an increased natural killer activity after ***IL***-***2*** treatment, and TNF

was increased in BAL fluid. Pulmonary function tests evidenced an increased alveolar-arterial difference for oxygen allied with a decrease of forced expiratory volume in 1 second, forced vital capacity, and carbon monoxide transfer coefficient consistent with a significant, albeit not clinically relevant, interstitial lung defect. Conclusion. Continuous- infusion ***IL***-***2*** is feasible in patients with advanced lung cancer even outside an intensive care unit, but overall compliance is poor. Although clinical pulmonary toxicity is negligible, small but statistically significant alterations of the pulmonary function are evident. In addition, this regimen produces a significant activation of the immune system at the pulmonary level.

12/7/26 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE
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9129268 EMBASE No: 94077347
Intravenous lipids - Depression of the immune function: Fact or fantasy? Hardin T.C.
Clinical Coordinator, Pharmacy Service, Audie L. Murphy Memorial Vet. Hosp., 7400 Merton Menter Blvd, San Antonio, TX 78284 USA HOSP. PHARM. (USA) , 1994, 29/2 (182+185-186+189) CODEN: HOPHA ISSN: 0018-5787
LANGUAGES: English SUMMARY LANGUAGES: English
Early research demonstrated that intravenously administered lipids do have the potential to depress immune function by impairing leukocyte function, blocking RES function, and altering cell-mediated immunity. Much of this work however, has been conducted in studies using bolus administration of large amounts of lipid emulsion. The immunological effects of more conservative dosages administered as a continuous infusions over 12-24 hours/day are less clear. The proposed mechanisms for intravenous lipids to act as immunomodulators are varied. As the chylomicron-like lipid is metabolized, increased triglyceride concentrations may alter the function of macrophages by reducing chemotaxis and phagocytic capacity, although this has not been consistently demonstrated. Excessive parenteral administration of lipid may overload the mononuclear cells of the RES, resulting in an inability to clear bacteria from the bloodstream. Clearly, lipid-associated reductions in the clearance of ***colloidal*** markers have been described. Studies assessing the alterations in cellular immunity associated with intravenous infusions of lipid emulsions have produced mixed results. Some authors have reported increases in B-lymphocyte and T-lymphocyte counts, increased lymphocyte mitogenesis, and increased production of ***interleukin***-***2*** (***IL***-***2***) in patients receiving parenteral lipids. Others have reported either no change or decreases in natural-killer cell counts, helper-to-suppressor cell ratios, and antibody dependent cellular cytotoxicity when compared to patients not receiving intravenous lipids. Further, interpretation of these studies and application of these findings is problematic due to questionable methodologies, variations in the amount and administration of the lipid and inconsistent outcome parameters. To date, no significant changes in serum immunoglobulin or complement concentrations have been observed secondary to intravenous lipid administration. Much of the earlier work was performed to demonstrate immunological response differences in patients receiving commercially available intravenous lipid emulsions as compared to patients receiving no parenteral lipid. A growing area of interest as lipids are evaluated for immunomodulatory activity is the clinical use of intravenous medium-chain triglyceride (MCT) containing products. MCTs have very different metabolic fates than the long-chain triglycerides and may not demonstrate similar detrimental effects on the function of the RES, leukocyte activity, and eicosanoid production. Another focus of research is the differences observed between the various lipid components and fatty acids. The polyunsaturated fatty acid (PUFA) content of cell membranes is an important factor in the structural and functional integrity of the cell, and this content can be altered by the provision of increased amounts of n-3 fatty acids in place of n-6 fatty acids. The incorporation of eicosapentaenoic acid, an example of n-3 fatty acids, into macrophages has been shown to reduce release of TNF, interleukin, and eicosanoids from cells stimulated with endotoxin. Further in vitro work has confirmed that the products of eicosapentaenoic acid (20:5n-3) are less inflammatory than those of linoleic acid (18:2n-6). The clinical significance of these findings must await further investigation.

12/7/27 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE
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8367771 EMBASE No: 92043476
Parenteral delivery systems for proteins
Hora M.S.
Formulation and Pharmaceutical Development, Cetus Corp., 1400 53 Rd St., Emeryville, CA 94608 USA
DRUG NEWS PERSPECT. (Spain) , 1991, 4/9 (538-543) CODEN: DNPEE ISSN: 0214-0934
LANGUAGES: English

12/7/28 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1995 Elsevier Science B.V. All rts. reserv.

6256534 EMBASE No: 86251597
Results of clinical trials with the administration of ***interleukin*** ***2*** and adoptive immunotherapy with activated cells in patients with cancer
Lotze M.T.; Rosenberg S.A.
Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892 USA
IMMUNOBIOLOGY (GERMANY, WEST) , 1986, 172/3-5 (420-437) CODEN: ZIMMD LANGUAGES: ENGLISH
The administration of transferred lymphokine-activated killer (LAK) cells in conjunction with the administration of recombinant ***interleukin*** ***2*** (***IL*** ***2***) at high doses has led to objective remissions in 14/41 cancer patients. Sequential studies with both Jurkat-derived ***IL*** ***2***, recombinant ***IL*** ***2*** and activated cells were conducted in a total of sixty-seven patients with cancer which established the safety, toxicity and immunologic effects of these treatments prior to their successful combination in humans. This regimen was developed in pulmonary and hepatic metastases models in mice using a variety of transplantable tumors. More recently we have demonstrated both in mice and in patients with melanoma that very high doses of recombinant ***IL*** ***2*** (> 100,000 units/kg administered three times daily) can lead to objective regressions. The future development of these immunotherapies will include their evaluation in adjuvant settings as well as in combination with other conventional cancer treatments.
?display sets

Set	Items	Description
S1	85401	INTERLEUKIN(W)2 OR IL(W)2 OR IL2
S2	5529	S1 AND TOXIC?
S3	1392	S2 AND ANTIBOD?
S4	627	S1 AND TOXIC?/TI
S5	19	S4 AND ANTIBOD?/TI
S6	15	RD (unique items)
S7	84894	INTERLEUKIN(W)2 OR IL(W)2 OR IL2/TI
S8	623	S7 AND TOXIC?/TI
S9	19	S8 AND ANTIBOD?/TI
S10	15	RD (unique items)
S11	53	S1 AND COLLOID?
S12	28	RD (unique items)

?s s1 and (colloid?(w)gold)

85401 S1
40116 COLLOID?

```
        47505  GOLD
         6030  COLLOID?(W)GOLD
   S13     24  S1 AND (COLLOID?(W)GOLD)
?rd

...completed examining records
   S14     10  RD (unique items)
?t s14/6/1-10


?s s1 and (silver or gold or iron or aluminum)

>>> PAUSE ended.
        85401  S1
        48426  SILVER
        47505  GOLD
       157856  IRON
        45400  ALUMINUM
   S15    447  S1 AND (SILVER OR GOLD OR IRON OR ALUMINUM) ?td

>>>Direct TYPE is available "FROM" a single file only
?rd

...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...examined 50 records  (300)
...examined 50 records  (350)
...examined 50 records  (400)
...completed examining records
   S16    262  RD (unique items)
?t s16/6/1-30


?t s16/7/18


 16/7/18     (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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08860938   94175938
  Effects of ***gold*** on ***interleukin***-***2*** and ***interleukin***- ***2*** receptor: comment on
the article by Sfikakis et al [letter; comment]
  Harth M
  Arthritis Rheum (UNITED STATES)  Jan 1994,  37 (1) p147,  ISSN 0004-3591 Journal Code: 90M
  Comment on  Arthritis Rheum 1993 Feb;36(2):208-12
  Languages: ENGLISH
  Document type: COMMENT; LETTER
?display sets
```

Set Items Description
S1 85401 INTERLEUKIN(W)2 OR IL(W)2 OR IL2
S2 5529 S1 AND TOXIC?
S3 1392 S2 AND ANTIBOD?
S4 627 S1 AND TOXIC?/TI
S5 19 S4 AND ANTIBOD?/TI
S6 15 RD (unique items)
S7 84894 INTERLEUKIN(W)2 OR IL(W)2 OR IL2/TI
S8 623 S7 AND TOXIC?/TI
S9 19 S8 AND ANTIBOD?/TI
S10 15 RD (unique items)
S11 53 S1 AND COLLOID?
S12 28 RD (unique items)
S13 24 S1 AND (COLLOID?(W)GOLD)
S14 10 RD (unique items)
S15 447 S1 AND (SILVER OR GOLD OR IRON OR ALUMINUM) S16 262 RD (unique items)
?s s7 and gold/ti

84894 S7
13279 GOLD/TI
S17 45 S7 AND GOLD/TI
?rd

...completed examining records
S18 24 RD (unique items)
?t s18/6/1-24

t s18/7/6,9,10,21

18/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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08449451 93159451
Suppression of ***interleukin***-***2*** and ***interleukin***-***2*** receptor biosynthesis by ***gold*** compounds in in vitro activated human peripheral blood mononuclear cells [see comments]
Sfikakis PP; Souliotis VL; Panayiotidis PP
First Department of Internal Medicine, Athens University Medical School, Laikon Hospital, Greece.
Arthritis Rheum (UNITED STATES) Feb 1993, 36 (2) p208-12, ISSN 0004-3591 Journal Code: 90M
Comment in Arthritis Rheum 1994 Jan;37(1):147
Languages: ENGLISH
Document type: JOURNAL ARTICLE
OBJECTIVE. To further investigate the mechanism of action of gold compounds by studying their effects on ***interleukin***-***2*** (***IL***- ***2***) and ***IL***-***2*** receptor (IL-2R) biosynthesis. METHODS. We cultured phytohemagglutinin- or anti-CD3 antibody-activated normal peripheral blood mononuclear cells (PBMC), as well as the erythroleukemic K562 cell line, in the presence of gold sodium thiomalate or auranofin. Tritiated thymidine incorporation assays, cytotoxicity assays, immunofluorescence analysis, enzyme-linked immunosorbent assay, Northern blot, and RNA dot-blot hybridization were used. RESULTS. Gold compounds, at concentrations attainable in vivo, inhibited the proliferation of normal PBMC, with no evidence of direct cytotoxicity. This inhibitory effect was associated with a dose-dependent suppression of both ***IL***-***2*** and IL-2R messenger RNA accumulation. In

contrast, the same concentrations of gold compounds failed to inhibit the spontaneous proliferation of the ***IL***-***2*** -independent K562 cells. CONCLUSION. Our findings suggest an ***IL***-***2***/IL-2R-mediated mechanism for suppression of lymphocyte proliferation by gold compounds, which might account for the immunomodulatory effects of gold in patients with rheumatoid arthritis.

18/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06517940 88162940
Inhibition of in vitro proliferative response of cultured T lymphocytes to ***interleukin***-***2*** by ***gold*** sodium thiomalate. Wolf RE; Hall VC
Department of Medicine, Louisiana State University Medical Center, Shreveport 71130.
Arthritis Rheum (UNITED STATES) Feb 1988, 31 (2) p176-81, ISSN 0004-3591 Journal Code: 90M
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Gold sodium thiomalate (GST), in concentrations attainable during chrysotherapy for rheumatoid arthritis, significantly inhibited the proliferative responses of cultured T cells stimulated by ***interleukin*** -***2*** (***IL***-***2***). The observed suppression was not related to altered kinetics, cell death, or interference with the binding of ***IL***- ***2*** to cell surface receptors. It appeared that GST affected an early step in the proliferative process, since maximum inhibition was obtained by the addition of GST within 4 hours of stimulation; progressive reduction of suppression was observed when GST was added later. Significant inhibition occurred when cultured T cells were preincubated for 24 hours with GST and washed prior to ***IL***-***2*** stimulation, although the degree of suppression was decreased. Thus, inhibitory activity was not dependent on the continued presence of GST throughout culture. These findings suggest that there is a direct inhibition of T lymphocytes by GST, which may be important in immunomodulation by gold compounds.

18/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06496179 88141179
Effects of ***gold*** on the production of and response to human interleukin-1.
Drakes ML; Harth M; Galsworthy SB; McCain GA
Department of Microbiology and Immunology, University of Western Ontario, London, Canada.
J Rheumatol (CANADA) Dec 1987, 14 (6) p1123-7, ISSN 0315-162X Journal Code: JWX
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We studied the effects in vitro of sodium aurothiomalate (GSTM) on the production of, and response to, a monocyte supernatant with interleukin-1 (IL-1)-like activity. Monocyte supernatant was produced by human peripheral blood monocytes stimulated with lipoprotein polysaccharide, and its IL-1-like activity assayed by its effect on tritiated thymidine incorporation by C3H/HeJ mouse thymocytes. GSTM inhibited the thymocyte response to monocyte supernatant even when added to monocyte supernatant and thymocytes after 48 h of culture. GSTM also inhibited production of IL-1-like activity by monocytes, when added to culture within the first 22 h. Inhibition of both response to and production of monocyte supernatant was dose dependent. These effects of GSTM on Il-1-like activity may constitute one of the mechanisms of action of the drug in rheumatoid arthritis.

18/7/21 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE
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9087119 EMBASE No: 94035283
Effects of ***gold*** on ***interleukin***-***2*** and ***interleukin***- ***2*** receptor: Comment on the article by Sfikakis et al (1) Harth M.; Sfikakis P.P.; Panayotidis P.
University of Western Ontario, London, Ont. Canada
ARTHRITIS RHEUM. (USA) , 1994, 37/1 (147) CODEN: ARHEA ISSN: 0004-3591 LANGUAGES: English

?s s7 and (antibod? and neutraliz?)

```
        84894  S7
      1114734  ANTIBOD?
        72092  NEUTRALIZ?
   S19   1307  S7 AND (ANTIBOD? AND NEUTRALIZ?)
```

?s s7 and (antibod? and biological(w)activity?)

```
Processing
        84894  S7
      1114734  ANTIBOD?
       673606  BIOLOGICAL
      2152856  ACTIVITY?
        41042  BIOLOGICAL(W)ACTIVITY?
   S20    156  S7 AND (ANTIBOD? AND BIOLOGICAL(W)ACTIVITY?) ?s s7 and (antibod? and
neutraliz?)/ti

        84894  S7
       317095  ANTIBOD?/TI
        12572  NEUTRALIZ?/TI
   S21     57  S7 AND (ANTIBOD? AND NEUTRALIZ?)/TI
```

?rd

```
...examined 50 records (50)
...completed examining records
   S22     23  RD (unique items)
```

?t s22/6/1-23

?s (interleukin(w)2 or il(w)2 or il2)/ti

```
Processing
Processing
Processing
        62059  INTERLEUKIN/TI
       675074  2/TI
        23815  INTERLEUKIN/TI(W)2/TI
        49415  IL/TI
       675074  2/TI
         8203  IL/TI(W)2/TI
          947  IL2/TI
   S23   31491  (INTERLEUKIN(W)2 OR IL(W)2 OR IL2)/TI
```

?display sets

```
Set     Items   Description
S1      85401   INTERLEUKIN(W)2 OR IL(W)2 OR IL2
S2       5529   S1 AND TOXIC?
S3       1392   S2 AND ANTIBOD?
S4        627   S1 AND TOXIC?/TI
S5         19   S4 AND ANTIBOD?/TI
S6         15   RD (unique items)
S7      84894   INTERLEUKIN(W)2 OR IL(W)2 OR IL2/TI
S8        623   S7 AND TOXIC?/TI
S9         19   S8 AND ANTIBOD?/TI
S10        15   RD (unique items)
S11        53   S1 AND COLLOID?
S12        28   RD (unique items)
S13        24   S1 AND (COLLOID?(W)GOLD)
S14        10   RD (unique items)
S15       447   S1 AND (SILVER OR GOLD OR IRON OR ALUMINUM) S16      262   RD (unique items)
S17        45   S7 AND GOLD/TI
S18        24   RD (unique items)
S19      1307   S7 AND (ANTIBOD? AND NEUTRALIZ?)
S20       156   S7 AND (ANTIBOD? AND BIOLOGICAL(W)ACTIVITY?) S21       57   S7 AND
(ANTIBOD? AND NEUTRALIZ?)/TI
S22        23   RD (unique items)
S23     31491   (INTERLEUKIN(W)2 OR IL(W)2 OR IL2)/TI
S24        15   S23 AND (NEUTRALIZ? AND ANTIBOD?)/TI
S25         8   RD (unique items)
?s s 23 and toxic?


  ?s s 23 and toxic?/ti

           0  S 23
      161830  TOXIC?/TI
    S26       0  S 23 AND TOXIC?/TI
?s s23 and toxic?/ti

       31491  S23
      161830  TOXIC?/TI
    S27     386  S23 AND TOXIC?/TI
?s s27 and antibod?/ti

         386  S27
      317095  ANTIBOD?/TI
    S28       8  S27 AND ANTIBOD?/TI
?rd

...completed examining records
    S29       6  RD (unique items)
?t s29/6/1-6


 29/6/1     (Item 1 from file: 155)
06778480   89080480
   ***Toxicity*** and therapeutic efficacy of high-dose ***interleukin*** ***2***. In vivo infusion of
***antibody*** to NK-1.1 attenuates ***toxicity*** without compromising efficacy against murine leukemia.
```

29/6/2 (Item 1 from file: 5)
10229283 BIOSIS Number: 45029283
ANTI-CD3 ANTI-***IL2*** RECEPTOR CD3 25 BISPECIFIC MONOCLONAL ***ANTIBODY*** BSMAB PROLONGATION OF CARDIAC ALLOGRAFT SURVIVAL WITH LOWER ***TOXICITY*** THAN ANTI-CD3 MAB

29/6/3 (Item 2 from file: 5)
10228935 BIOSIS Number: 45028935
ANTI-CD3 ANTI-***IL***-***2*** RECEPTOR CD3 25 BISPECIFIC MONOCLONAL ***ANTIBODY*** BSMAB T CELL IMMUNOMODULATION WITH REDUCED ACTIVATION AND ***TOXICITY*** THAN ANTI-CD3 MAB IN-VIVO

29/6/4 (Item 3 from file: 5)
4068719 BIOSIS Number: 76018570
CORD IMMUNO GLOBULIN M ***ANTIBODY*** SPECIFIC FOR HUMAN KILLER T CELLS T LYMPHOCYTO ***TOXIC*** HUMAN FETAL ***ANTIBODY*** RECOGNIZING MATERNAL KILLER T CELLS PROLIFERATING IN THE PRESENCE OF ***INTERLEUKIN*** ***2***

29/6/5 (Item 4 from file: 5)
3826563 BIOSIS Number: 24033922
THE BIOCHEMISTRY BIOLOGY AND ROLE OF ***INTERLEUKIN*** ***2*** IN THE INDUCTION OF CYTO ***TOXIC*** T CELL AND ***ANTIBODY*** FORMING B CELL RESPONSES

29/6/6 (Item 5 from file: 5)
3647013 BIOSIS Number: 73039380
THE ROLE OF ***INTERLEUKIN*** ***2*** IN THE DIFFERENTIATION OF CYTO ***TOXIC*** T CELLS THE EFFECT OF MONO CLONAL ANTI ***INTERLEUKIN*** ***2*** ***ANTIBODY*** AND ABSORPTION WITH ***INTERLEUKIN*** ***2*** DEPENDENT T CELL LINES
?s colloid?(w)gold and carrier?

```
        40116  COLLOID?
        47505  GOLD
         6030  COLLOID?(W)GOLD
       142863  CARRIER?
   S30     65  COLLOID?(W)GOLD AND CARRIER?
```
?s s30 and (vaccin? or immuniz?)

```
           65  S30
       241925  VACCIN?
       151947  IMMUNIZ?
   S31      0  S30 AND (VACCIN? OR IMMUNIZ?)
```
?rd s30

...examined 50 records (50)
...completed examining records
S32 38 RD S30 (unique items)
?t s32/6/1-38

?t s32/7/9,20

32/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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07927580 92065580
Production of anti-platelet-activating factor antibodies by the use of ***colloidal*** ***gold*** as ***carrier***.
Tomii A; Masugi F
Department of Medicine and Geriatrics, Osaka University Medical School, Japan.
Jpn J Med Sci Biol (JAPAN) Apr 1991, 44 (2) p75-80, ISSN 0021-5112 Journal Code: KLZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Polyclonal and monoclonal antibodies to platelet-activating factor (PAF) were produced, by use of ***colloidal*** ***gold*** as the hapten ***carrier*** . These polyclonal (R88-09) and monoclonal (602 B11) antibodies both reacted with PAF, lysoplatelet-activating factor (lyso PAF), and L-alpha-lysophosphatidylcholine, palmitoyl (lyso PCP), but did not react with phosphorylcholine chloride (PCC). Their affinities were higher for PAF than lyso PAF and lyso PCP.

32/7/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06027412 87001412
A new method for producing a specific and high titre antibody against glutamate using ***colloidal*** ***gold*** as a ***carrier***. Shiosaka S; Kiyama H; Wanaka A; Tohyama M
Brain Res (NETHERLANDS) Sep 24 1986, 382 (2) p399-403, ISSN 0006-8993 Journal Code: B5L
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Antiserum against the glutamate was developed using ***colloidal*** ***gold*** as a ***carrier*** for the antigen. Glutamate was bound directly to ***colloidal*** ***gold*** without using cross-linking reagents such as glutaraldehyde, formaldehyde, or carbodiimide. Repeated injection of the ***colloidal*** ***gold*** -glutamate complex into the rabbit yielded a specific, high titre antiserum. Specificity was verified by radioimmunoassay and histochemically with absorption controls. The antiserum immunohistochemically detected numerous glutamate-containing neurons in the rat brain.
?s colloid?(w)gold and (vaccin? or immuniz?)

```
     40116  COLLOID?
     47505  GOLD
      6030  COLLOID?(W)GOLD
    241925  VACCIN?
    151947  IMMUNIZ?
S33    110  COLLOID?(W)GOLD AND (VACCIN? OR IMMUNIZ?) ?rd

...examined 50 records (50)
...examined 50 records (100)
...completed examining records
S34     67  RD (unique items)
?t s34/6/1-67
```

?s colloid?(w)gold and (cancer? or tumor?)

Processing

40116 COLLOID?
47505 GOLD
6030 COLLOID?(W)GOLD
1098711 CANCER?
1058243 TUMOR?
S35 384 COLLOID?(W)GOLD AND (CANCER? OR TUMOR?)
?s colloid?(w)gold/ti and (cancer? or tumor?)

Processing
10513 COLLOID?/TI
13279 GOLD/TI
1399 COLLOID?/TI(W)GOLD/TI
1098711 CANCER?
1058243 TUMOR?
S36 85 COLLOID?(W)GOLD/TI AND (CANCER? OR TUMOR?) ?rd

...examined 50 records (50)
...completed examining records
S37 69 RD (unique items)
?t s37/6/1-69

?t s37/7/5,8,9,11,15,16

37/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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07753004 91272004
Combined treatment of lung ***cancer*** using radioactive ***colloid*** ***gold*** in the postoperative period|
Kombinirovannoe lechenie raka legkogo s ispol'zovaniem radio- aktivnogo kolloidnogo zolota v posleoperatsionnom periode.
Ias'kevich LS
Sov Med (USSR) 1990, (12) p100-4, ISSN 0038-5077 Journal Code: UW7 Languages: RUSSIAN
Document type: JOURNAL ARTICLE

37/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1995 Knight-Ridder Info. All rts. reserv.

06918042 89220042
Further facts in pleural recurrence prevention by radio-***colloidal*** ***gold*** in operated breast ***cancer***|
Weitere Fakten zur Rezidivprophylaxe der Pleuren beim operierten Brustkrebs mittels kolloidalen Radiogoldes.
Sattler A
Osterr Z Erforsch Bekampf Krebskr (AUSTRIA) 1970, 25 (1) p6-23, ISSN 0300-8703 Journal Code: OMW
Languages: GERMAN Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract
The communication deals with endoscopical facts making recognizable that the intrapleural incorporation of

colloidal radio-gold after the so-called radical mastectomy corresponds to a preventive-curative act. There is an analysis and proof of lymphogenous nature of the threatening, in it's manifest stage always lethal early and late pleural metastasis. The special and various features of the pleural cavity in postoperative endoscopy are demonstrated as a basis for the following dosage of radio-gold in a preventive-curative sense. Original, spectacular pictures are represented. On the basis of an experience for decades and because of the insufficient results of surgical therapy and conventional radiotherapy, unsatisfactory quoad sanationem et vitam, it must be pointed out that an additional, intrapleural radio-gold therapy is imperative. The application must be done early after operation. The effectiveness of this application is beyond question, since the pioneer-work of J. H. Muller and the ten years results with his preoperative radio-gold infiltration of the breast and my own endoscopically developed intrapleural radio-gold infusion. Both methods make possible true healing and ten years survival. For this reasons I recommend the employ of the more practicable intrapleural infusion on a big collective. The question of a long-term effectiveness of the therapy with fast electrons (betatron) is still to be decided on the ten years parameter. But I don't doubt that radio-gold is superior to all kind of radiotherapy controlling the contralateral pleural dissemination.

37/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06799978 89101978
Use of radioactive ***colloidal*** ***gold*** (Au-198) in the combined treatment of ***cancer*** of the rectum]
Primenenie radioaktivnogo kolloidnogo zolota (198Au) pri kombinirovannom lechenii raka priamoi kishki.
Knysh VI; Barsukov IuA; Kokhniuk VT
Vestn Akad Med Nauk SSSR (USSR) 1988, (6) p35-8, ISSN 0002-3027 Journal Code: X9A
Languages: RUSSIAN Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract

37/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06509387 88154387
Preparation and characterization of a ***colloidal*** ***gold***-insulin complex with binding and biological activities identical to native insulin. Smith RM; Goldberg RI; Jarett L
Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia 19104.
J Histochem Cytochem (UNITED STATES) Apr 1988, 36 (4) p359-65, ISSN 0022-1554 Journal Code: IDZ
Contract/Grant No.: DK 28143; DK 19525
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We studied the binding and biological activities of gold-insulin complexes to develop a complex with properties identical to native insulin. Stabilizing amounts of insulin absorbed to 5-, 10-, or 15-nm gold particles resulted in complexes with 40-327 insulin molecules per gold particle and 4-111 times the biological activity of unlabeled insulin, based on the molar concentration of gold complex. These data suggested that these complexes behaved as multivalent ligands. Gold-insulin complexes were prepared with 5% of the stabilizing insulin concentration and were stabilized with bovine serum albumin. This resulted in a complex with 5-7 insulin molecules per 10-nm gold particle, which stimulated glucose oxidation in rat adipocytes and competed with [125I]-insulin for binding to the insulin receptor identically to unlabeled insulin on an equimolar basis. The organization and distribution of insulin receptors occupied by this monovalent-behaving gold-insulin complex were virtually identical to previous observations using monomeric ferritin-insulin. Since multivalent ligands may affect receptor binding, re-distribution, and intracellular processing, the use of

electron-dense probes that resemble the unlabeled ligand in biological and binding properties is appropriate when studying receptor dynamics of in vivo or in vitro biological systems. The gold-insulin complex developed in this study should serve this function.

37/7/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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04458762 82001762
Radioactive ***colloidal*** ***gold*** in the treatment of endometrial ***cancer***: Mayo Clinic experience, 1952-1976.
Fountain KS; Malkasian GD Jr
Cancer (UNITED STATES) May 15 1981, 47 (10) p2430-2, ISSN 0008-543X Journal Code: CLZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A review of 1670 patients with endometrial ***cancer*** who were treated between 1952 and 1976 revealed that 15 patients had received radioactive colloidal gold as an adjunct to surgery. Most of the patients had follow-up more than ten years, and all had microscopic ***tumor*** contamination of the peritoneal cavity. Of the 15 patients, 13 had biopsy of peritoneal metastases and underwent resection of gross metastatic lesions that were more than 2 mm in diameter. The other two patients had direct extension of the ***tumor*** through the uterus into the peritoneal cavity without visible metastasis. The radiogold was inserted from 4-37 days after the initial surgical procedure. The dosage ranged from 100-140 mCi. At follow-up, from 11 years seven months to 24 years two months after treatment, seven patients were alive without evidence of disease. Three died of intercurrent disease, 16 years, and 14 years, and 14 years two months after treatment. Five patients died of ***cancer***, two with local recurrence and three with distant metastases to lung or bone (or both).

37/7/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1995 Knight-Ridder Info. All rts. reserv.

03021324 76202324
Treatment of malignant ovarian ***tumors*** with radioactive ***colloidal*** ***gold***.
Nishimura A; Sugimori H; Taki I
Acta Obstet Gynaecol Jpn (JAPAN) Jul 1974, 21 (3) p170-5, ISSN 0001-6330 Journal Code: 1E2
Languages: ENGLISH
Document type: JOURNAL ARTICLE

File 351:DERWENT WPI 1981-1995/UD=9524;UA=9518;UM=9514
(c)1995 Derwent Info Ltd

Set Items Description
--- ----- -----
?s interleukin(w)2 or il(w)2 or il2

1404 INTERLEUKIN
2091760 2
548 INTERLEUKIN(W)2
2728 IL
2091760 2
548 IL(W)2
63 IL2
S1 840 INTERLEUKIN(W)2 OR IL(W)2 OR IL2
?s s1 and colloid?

840 S1
14905 COLLOID?
S2 1 S1 AND COLLOID?
?t s2/6/1

2/6/1
009221507 WPI Acc No: 92-348930/42
Related WPI Accession(s): 93-152622; 93-153956
XRAM Acc No: C92-154873
New peat derived prods. contg. not more than 70 per cent inorganic salts - produced by dilution of salt contg. peat prod. with demineralised water followed by reverse osmosis, concn. and clarification used in pharmaceuticals and cosmetics
?logoff hold

File 155:MEDLINE(R) 1966-1995/Aug W4
(c) format only 1995 Knight-Ridder Info

Set Items Description
--- ----- -----------
?s (interleukin(w)2 and neutraliz? and antibod?)/ti

17468 INTERLEUKIN/TI
151882 2/TI
6830 INTERLEUKIN/TI(W)2/TI
4079 NEUTRALIZ?/TI
102673 ANTIBOD?/TI
S1 3 (INTERLEUKIN(W)2 AND NEUTRALIZ? AND ANTIBOD?)/TI ?xD

?t s1/6/1-3

1/6/1
07649066 91168066
The development of ***neutralizing*** ***antibodies*** in a patient receiving subcutaneous recombinant and natural ***interleukin***-***2***.

1/6/2
06902465 89204465
Production and use of ***neutralizing*** monoclonal ***antibodies*** to rat ***interleukin***-***2***.

1/6/3
06307680 87281680
Neutralizing monoclonal ***antibodies*** against recombinant human ***interleukin***-***2***.
?t s1/7/1

1/7/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1995 Knight-Ridder Info. All rts. reserv.

07649066 91168066
The development of ***neutralizing*** ***antibodies*** in a patient receiving subcutaneous recombinant and natural ***interleukin***-***2***. Kirchner H; Korfer A; Evers P; Szamel MM; Knuver-Hopf J; Mohr H; Franks CR; Pohl U; Resch K; Hadam M; et al
Department of Hematology & Oncology, MHH University Medical Center, Hanover, Germany.
Cancer (UNITED STATES) Apr 1 1991, 67 (7) p1862-4, ISSN 0008-543X Journal Code: CLZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Systemic administration of interleukin-2 (IL-2) in humans may induce antibodies specific to IL-2. The case is reported of a patient with metastatic rectal carcinoma who was treated with long-term subcutaneous IL-2 and a combination of subcutaneous IL-2 and interferon-alpha 2b (IFN-alpha 2b). This patient developed nonneutralizing and neutralizing anti-IL-2 antibodies recognizing both the recombinant and natural cytokine. Detectable serum levels of neutralizing antibodies were accompanied by the inhibition of immune responsiveness to systemic IL-2 in vivo. ?logoff hold

pinocytosis or secretion of growth factors or enzymes by pancreas tumour cells
?display sets

Set Items Description
S1 487634 COLLOID? OR GOLD OR METAL
S2 559038 COLLOID? OR GOLD OR METAL?
S3 77 S2 AND INTERFERON?
S4 14905 COLLOID?
S5 7 S4 AND INTERFERON?
S6 3 S4 AND INTERLEUKIN?
S7 1 S4 AND (LIPID(W)A)
S8 3 S4 AND PHOSPHOLIPASE?
S9 6 S4 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS) S10 0 S4 AND ENTEROTOXIN
S11 1 S4 AND ENTEROTOXIN?
S12 3 S4 AND (TUMOR(W)NECROSIS(W)FACTOR? OR TNF??) S13 1 S4 AND (TRANSFORMING(W)GROWTH(W)FACTOR? OR TGF??) S14 0 S4 AND LYMPHOTOXIN?
S15 0 S4 AND (MIGRATION(W)INHIBITION(W)FACTOR? OR MIF??) S16 7 S4 AND (COLONY(W)STIMULATING(W)FACTOR? OR CSF??) S17 0 S4 AND (VASCULAR(W)ENDOTHELIAL(W)GROWTH(W)FACTOR? OR VEGF?- ?)
S18 1 S4 AND ANGIOGENIN
S19 1 S4 AND (HEAT(W)SHOCK(W)PROTEIN? OR HSP?)
S20 0 S4 AND (BLOOD(W)GROUP?)
S21 173 S4 AND (RH)
S22 0 S4 AND RH(W)FACTOR?
S23 1 S4 AND (FIBROBLAST(W)GROWTH(W)FACTOR? OR FGF?) ?logof fhold`

>>>Invalid set number

File 351:DERWENT WPI 1981-1995/UD=9524;UA=9518;UM=9514
(c)1995 Derwent Info Ltd

Set Items Description
--- ----- -----------
?s colloid? or gold or metal

14905 COLLOID?
12322 GOLD
468267 METAL
S1 487634 COLLOID? OR GOLD OR METAL
?s colloid? or gold or metal?

14905 COLLOID?
12322 GOLD
540849 METAL?
S2 559038 COLLOID? OR GOLD OR METAL?
?s s2 and interferon?

559038 S2
2040 INTERFERON?
S3 77 S2 AND INTERFERON?
?s colloid?

S4 14905 COLLOID?
?s s4 and interferon?

14905 S4
2040 INTERFERON?
S5 7 S4 AND INTERFERON?
?t s5/6/1-7

5/6/1
010152195 WPI Acc No: 95-053447/08
XRAM Acc No: C95-024314
Improving oral bio-availability of drugs - by applying cationic coating of polysaccharide to provide bio-adhesive action to negatively charged mucous mucosa

5/6/2
010048952 WPI Acc No: 94-316663/39
XRAM Acc No: C94-144254
Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. interleukin, has reduced toxic side effects, useful in vaccines and for treating cancer or immune disease

5/6/3
009768651 WPI Acc No: 94-048502/06
XRAM Acc No: C94-021879
Targetted drug delivery for lymphatic system - using ***colloidal*** carrier particles of controlled hydrophobicity, giving high uptake in prim. and sec. lymph nodes.

5/6/4
009221507 WPI Acc No: 92-348930/42
Related WPI Accession(s): 93-152622; 93-153956
XRAM Acc No: C92-154873
New peat derived prods. contg. not more than 70 per cent inorganic salts - produced by dilution of salt contg. peat prod. with demineralised water followed by reverse osmosis, concn. and clarification used in pharmaceuticals and cosmetics

5/6/5
008629879 WPI Acc No: 91-133909/19
XRAM Acc No: C91-057699
Improving bioavailability of peptide type pharmaceuticals - by micronising then coating particles in protective ***colloid***

5/6/6
008324614 WPI Acc No: 90-211615/28
XRAM Acc No: C90-091391
Micro-encapsulation of bioactive substances by phase-sepn. - comprises dispersing substance in organic soln. of biocompatible polymer, adding phase separator and excess hardening agent

5/6/7
007797714 WPI Acc No: 89-062826/09
XRAM Acc No: C89-027714
New use of ethyl (plus)-apovincaminate - for treatment of demyelinisation clinical patterns of autoimmune origin, partic. multiple sclerosis
?t s5/7/3,7

5/7/3
DIALOG(R)File 351:DERWENT WPI
(c)1995 Derwent Info Ltd. All rts. reserv.

009768651 WPI Acc No: 94-048502/06
XRAM Acc No: C94-021879
Targetted drug delivery for lymphatic system - using ***colloidal*** carrier particles of controlled hydrophobicity, giving high uptake in prim. and sec. lymph nodes.
Patent Assignee: (UYNO-) UNIV NOTTINGHAM; (DANB-) DANBIOSYST UK LTD Author (Inventor): CHRISTY N; DAVIS S S; ILLUM L; MOGHIMI M Number of Patents: 005
Number of Countries: 023
Patent Family:

CC Number	Kind	Date	Week	
WO 9402122	A1	940203	9406	(Basic)
AU 9347175	A	940214	9425	
NO 9500238	A	950123	9515	
GB 2283422	A	950510	9522	
EP 652746	A1	950517	9524	

Priority Data (CC No Date): GB 9216082 (920728)
Applications (CC,No,Date): EP 93917936 (930728); WO 93GB1596 (930728); WO 93GB1596 (930728); AU 9347175 (930728); WO 93GB1596 (930728); WO 93GB1596 (930728); NO 95238 (950123); WO 93GB1596 (930728); GB 9563 (930728)
Language: English

EP and/or WO Cited Patents: 03Jnl.Ref
Designated States
(National): AU; CA; FI; GB; JP; NO; US
(Regional): BE; CH; DE; DK; ES; FR; GB; IE; IT; LI; PT; SE; AT; GR; LU; MC ; NL
Filing Details: EP0652746 Based on WO 9402122; AU9347175 Based on WO 9402122; GB2283422 Based on WO 9402122
Abstract (Basic): WO 9402122 A

Compsn. for delivering an active agent (A) to the lymphatic system comprises ***colloidal*** particles (I) each associated with (A), where (i) the surface of each particle has hydrophobicity ratio less than 10 (pref. less than 5); or (ii) a modifying agent (II) is absorbed onto or attached to the surface of each particle, such that (a) (II) gives an advancing contact angle of less than 60 deg. (b) the thickness of the (II) layer is 0.8-4.0mm, (c) the albumin uptake ratio (AUR) of the surface is 0.2-0.5 or (d) the thickness of the (II) layer is less than 10 (pref. 0.8-4.0) mm and hydrophobicity ratio is less than 5, advancing contact angle is less than 60 deg. or AUR is 0.2-0.5. Hydrophobicity ratio is measured by hydrophobic interaction chromatography using butyl agarose. Advancing contact angle is that obtd. when (II) is absorbed or attached to the surface of polystyrene at a concn. providing a plateau in the absorption isotherm. AUR is the ratio of the amt. of human serum albumin absorbed on test particles to the amt. absorbed on control polystyrene particles.

USE/ADVANTAGE - The compsn. is used for targeting diagnostic and therapeutic agents to the lymphatic system. Typical applications are: (a) imaging and visualisation (e.g. by lymphangiography, lymphoscintigraphy, CAT, MRI, or ultrasound) for detection of neoplasms, esp. of unaccessible nodes in patients with malignant diseases, where (A) is a contrast or imaging agent such as iron oxide, perfluoroalkyl bromide, Tc-99m, In-111, I-131, I-123, or Sm-153; (b) radiation therapy, using ***colloids*** labelled with Au-198 or Y-90 or oils labelled with I-131 for ablation of metastatic disease; or (c) delivery of drugs to lymph nodes, e.g. antimicrobial agents for treating filariasis, brucellosis, tuberculosis or HIV, antitumour agents, (e.g. mitomycin C, bleomycin or antibodies against tumours) and macrophage modifying agents (e.g. ***interferons***, MDP or cyclosporin). Modification of the surface hydrophobicity/hydrophilicity of (I) greatly increases the uptake of (I) in regional lymph nodes. Uptake is high in both prim. and sec. lymph nodes and (A) spread well from the injection site. The distribution in a rat foot pad model at 24 hrs. is typically less than 25% (A) remaining at the injection site, at least 20% in the prim. and sec. lymph nodes and at least 5% each in the prim. and sec. nodes. Dwg.0/4
Derwent Class: A96; B07;
Int Pat Class: A61K-009/18; A61K-009/51; A61K-049/02; A61K-051/12 Derwent Registry Numbers: 1850-U; 2044-U

5/7/7
DIALOG(R)File 351:DERWENT WPI
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007797714 WPI Acc No: 89-062826/09
XRAM Acc No: C89-027714

New use of ethyl (plus)-apovincaminate - for treatment of demyelinisation clinical patterns of autoimmune origin, partic. multiple sclerosis

Patent Assignee: (RICT) RICHTER GEDEON VEGY
Author (Inventor): BOZOKY B; FORGACS L; FRANK T; HAJOS G; SYPORNY L; SZEGVARI Z; TIGYI G; SZPORNY L
Number of Patents: 006
Number of Countries: 015
Patent Family:

CC Number	Kind	Date	Week	
EP 305181	A	890301	8909	(Basic)
JP 1071814	A	890316	8917	
US 4882336	A	891121	9005	

HU T52698	T	900828	9039
EP 305181	B1	941130	9501
DE 3852246	G	950112	9507

Priority Data (CC No Date): HU 873753 (870826)
Applications (CC,No,Date): DE 3852246 (880825); EP 88307883 (880825); EP 88307883 (880825); JP 88207472 (880823); US 233076 (880817); EP 88307883 (880825)
Language: English
EP and/or WO Cited Patents: 6.Jnl.Ref; A3...9034; No-SR.Pub; 03Jnl.Ref Designated States (Regional): AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; NL; SE Filing Details: DE3852246 Based on EP 305181
Abstract (Basic): EP 305181

The use is claimed of ethyl (+)-apovincaminate (I) in prepn. of a medicament for use in treatment of demyelinisation clinical patterns of autoimmune origin. Compsns. comprising (I) and other therapeutically active cpd(s). (II) are also claimed.

Prefd. (II) are those normally used for the above, from antiinflammatory agents, immunosuppressive agents and cytostatic agents, esp. steroids, cyclophosphamide, azathiprine, cyclosporin A and alpha-***interferon***. (I) is known from e.g. GB1405127. USE/ADVANTAGE - Partic. for treating multiple sclerosis, perivenous encephalomyelitis and acute haemorrhagic leukoencephalitis. (I) shows no toxic side effects at therapeutically effective doses in animal models. Doses of (I) are 0.05-50 mg/kg/day, opt. divided. In an example, tablets were prepd., each comprising 5.00mg (I), 1.25mg ***colloidal*** silicic acid, 2.50mg magnesium stearate, 5.00mg talc, 96.25mg starch and 140.00mg lactose. @(8pp Dwg.No.0/2)@ Abstract (US): 9005 US 4882336

The use is claimed of ethyl (+)-apovincaminate (I) in prepn. of a medicament for use in treatment of demyelinisation clinical patterns of autoimmune origin. Compsns. comprising (I) and other therapeutically active cpd(s). (II) are also claimed.

Prefd. (II) are those normally used for the above, from antitn flammatory agents, immunosuppressive agents and cytostatic agents, esp. steroids, cyclophosphamide, azathiprine, cyclosporin A and alpha- ***interferon***. (I) is known from e.g. GB1405127.

USE/ADVANTAGE - Partic. for treating multiple sclerosis, perivenous encephalomyelitis and acute haemorrhagic leukoencephalitis. (I) shows no toxic side effects at therapeutically effective doses in animal models. Doses of (I) are 0.05-50 mg/kg/day, opt. divided. In an example, tablets were prepd., each comprising 5.00mg (I), 1.25mg ***colloidal*** silicic acid, 2.50mg magnesium stearate, 5.00mg talc, 96.25mg starch and 140.00mg lactose.

Abstract (EP): 9501 EP 305181 B

Use of ethyl (+)-aprovinacaminate in the manufacture of a medicament for the treatment of demyelinization clinical patterns of autoimmune origin, and wherein the treatment does not comprise use of ethyl (+)-aprovincaminate as adjuvant. Dwg.0/0

Derwent Class: B02;
Int Pat Class: A61K-031/47; A61K-031/475; A61K-031/52; A61K-031/675; A61K-037/02
Derwent Registry Numbers: 0008-U; 1259-U
?

5/7/8
>>>Item 8 is not within valid item range
?t s5/7/5

5/7/5
DIALOG(R)File 351:DERWENT WPI
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008629879 WPI Acc No: 91-133909/19
XRAM Acc No: C91-057699

Improving bioavailability of peptide type pharmaceuticals - by micronising then coating particles in protective ***colloid*** Patent Assignee: (BADI) BASF AG; (BADI) BASF AG; (HORN/) HORN D Author (Inventor): HORN D; END L; SPENGLER R; KRAUSE H J; ELZNER J Number of Patents: 004
Patent Family:

CC Number	Kind	Date	Week	
DE 3936053	A	910502	9119	(Basic)
EP 425892	A	910508	9119	
CA 2028665	A	910429	9128	
JP 3151326	A	910627	9132	

Priority Data (CC No Date): DE 3936053 (891028)
Applications (CC,No,Date): EP 90119879 (901017); JP 90287356 (901026) Language: German
EP and/or WO Cited Patents: A3...9142; EP 169618; EP 276735 Designated States (Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; NL; SE Abstract (Basic): DE 3936053

The bioavailability of pharmaceuticals (I) contg. peptide bonds is improved by (1) dissolving (I) and opt. surfactant in a volatile, water-miscible organic solvent at 5-200 deg.C, opt. under elevated pressure, in less than 10 sec.; (2) precipitating from the resulting molecularly dispersed soln., ***colloidally*** disperse (I) by immediate rapid mixing with an aq. soln. or dispersion of a sol. or swellable ***colloid*** (and a surfactant if not already dissolved in the organic solvent) at 0-50 deg.C, and (3) the resulting dispersion is converted to a redispersible powder by conventional removal of solvent and dispersant.

USE/ADVANTAGE - In these formulations each microparticle of (I) is coated with a layer of ***colloid*** which protects it against degradation in the gastro-intestinal tract. This means that resorption and bioavailability are improved, so a small dose of (I) can product a relatively high plasma concn. Typical (I) include polypeptide antibiotics; TNF; ***interferon***; or inhibitors of rennin or angiotensin-converting enzyme. @(5pp Dwg.No.0/1)@
Derwent Class: B04; B07;
Int Pat Class: A61K-009/14; A61K-037/02
?s s4 and interleukin?

```
        14905  S4
         1522  INTERLEUKIN?
    S6      3  S4 AND INTERLEUKIN?
```

?t s6/6/1-3

6/6/1
010152195 WPI Acc No: 95-053447/08
XRAM Acc No: C95-024314
Improving oral bio-availability of drugs - by applying cationic coating of polysaccharide to provide bio-adhesive action to negatively charged mucous mucosa

6/6/2
010048952 WPI Acc No: 94-316663/39
XRAM Acc No: C94-144254
Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. ***interleukin***, has reduced toxic side effects, useful in vaccines and for treating cancer or immune disease

6/6/3
007282648 WPI Acc No: 87-279655/40
XRAM Acc No: C87-118766
Removing nucleic acid and endotoxin from soln. - by treatment with low mol. wt. chitosan, esp. for purifying protein such as tumour necrosis factor

?s s4 and (lipid(w)A)

Processing
Processing
Processing
Processing
14905 S4
7151 LIPID
3775010 A
239 LIPID(W)A
S7 1 S4 AND (LIPID(W)A)
?t s7/6/1

7/6/1
010048952 WPI Acc No: 94-316663/39
XRAM Acc No: C94-144254
Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. interleukin, has reduced toxic side effects, useful in vaccines and for treating cancer or immune disease
?s s4 and phospholipase?

14905 S4
612 PHOSPHOLIPASE?
S8 3 S4 AND PHOSPHOLIPASE?
?t s8/6/1-3

8/6/1
010118265 WPI Acc No: 95-019516/03
XRAM Acc No: C95-009019
Image available
Simplified purificn. of fat and oil to improved yield - by adding enough water to emulsify, converting phospholipid in fat and oil into water-soluble material contg. phosphoric gps., etc.

8/6/2
010048952 WPI Acc No: 94-316663/39
XRAM Acc No: C94-144254
Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. interleukin, has reduced toxic side effects, useful in vaccines and for treating cancer or immune disease

8/6/3
004155736 WPI Acc No: 84-301275/49
XRAM Acc No: C84-128251
XRPX Acc No: N84-224626
Determn. of analyte in specific fraction in biological fluid after immunochemical removal of other fractions contg. the analyte ?s s4 and (endotoxin? or lipopolysaccharide? or lps)

14905 S4
818 ENDOTOXIN?
374 LIPOPOLYSACCHARIDE?
204 LPS
S9 6 S4 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS) ?t s9/6/1-5

9/6/1
010070589 WPI Acc No: 94-338302/42
XRAM Acc No: C94-153996
Image available
Efficient removal of ***endotoxin*** from liq. contg. protein - comprises contacting liq. with granules of crosslinked chitosan at pH higher than isoelectric point of protein, used for purificn. of protein solns. for drugs

9/6/2
010048952 WPI Acc No: 94-316663/39
XRAM Acc No: C94-144254
Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. interleukin, has reduced toxic side effects, useful in vaccines and for treating cancer or immune disease

9/6/3
009384428 WPI Acc No: 93-077906/10
XRAM Acc No: C93-034334
Endotoxin adsorber having high binding capacity - comprises polyethyleneimine bonded to porous carrier, esp. polysaccharide

9/6/4
007282648 WPI Acc No: 87-279655/40
XRAM Acc No: C87-118766
Removing nucleic acid and ***endotoxin*** from soln. - by treatment with low mol. wt. chitosan, esp. for purifying protein such as tumour necrosis factor

9/6/5
004558437 WPI Acc No: 86-061781/09
XRAM Acc No: C86-026381
Stimulation of phagocytosis in blood stream by administering somatostatin to increase clearance of particles
?t s9/6/6

9/6/6
003682100 WPI Acc No: 83-42073K/18
XRAM Acc No: C83-040992
Filter of inorganic microfibres given positive zeta potential by coating with pptd. cured cationic thermoset binder
?s s4 and enterotoxin

```
        14905  S4
          122  ENTEROTOXIN
   S10      0  S4 AND ENTEROTOXIN
```

?s s4 and enterotoxin?

```
        14905  S4
          139  ENTEROTOXIN?
   S11      1  S4 AND ENTEROTOXIN?
```

?t s11/6/1

11/6/1
007689676 WPI Acc No: 88-323608/46
XRAM Acc No: C89-041479
Anti-diarrhoeal medicaments - contain 2-pyrrolidino-cyclohexyl 3-pentyl-oxy- carbanilate
?display sets

Set Items Description
S1 487634 COLLOID? OR GOLD OR METAL
S2 559038 COLLOID? OR GOLD OR METAL?
S3 77 S2 AND INTERFERON?
S4 14905 COLLOID?
S5 7 S4 AND INTERFERON?
S6 3 S4 AND INTERLEUKIN?
S7 1 S4 AND (LIPID(W)A)
S8 3 S4 AND PHOSPHOLIPASE?
S9 6 S4 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS) S10 0 S4 AND ENTEROTOXIN
S11 1 S4 AND ENTEROTOXIN?
?s s4 and (tumor(w)necrosis(w)factor? or tnf??)

14905 S4
396 TUMOR
1228 NECROSIS
53725 FACTOR?
25 TUMOR(W)NECROSIS(W)FACTOR?
708 TNF??
S12 3 S4 AND (TUMOR(W)NECROSIS(W)FACTOR? OR TNF??) ?t s12/6/1-3

12/6/1
009424222 WPI Acc No: 93-117738/14
XRAM Acc No: C93-052355
XRPX Acc No: N93-089700 *Image available*
Detecting bioactive tumour necrosis factor - using capturing reagent capable of reacting with oligomeric ***TNF*** but not with monomeric or receptor-complexed ***TNF***

12/6/2
008629879 WPI Acc No: 91-133909/19
XRAM Acc No: C91-057699
Improving bioavailability of peptide type pharmaceuticals - by micronising then coating particles in protective ***colloid***

12/6/3
007282648 WPI Acc No: 87-279655/40
XRAM Acc No: C87-118766
Removing nucleic acid and endotoxin from soln. - by treatment with low mol. wt. chitosan, esp. for purifying protein such as tumour necrosis factor
?s s4 and (transforming(w)growth(w)factor? or tgf??)

14905 S4
5244 TRANSFORMING

43029 GROWTH
53725 FACTOR?
241 TRANSFORMING(W)GROWTH(W)FACTOR?
262 TGF??
S13 1 S4 AND (TRANSFORMING(W)GROWTH(W)FACTOR? OR TGF??) ?t s13/6/1

13/6/1
007431204 WPI Acc No: 88-065139/10
XRAM Acc No: C88-029159
Tumour therapy with monoclonal antibodies or other ligands - which inhibit ***colloidal*** gold pinocytosis or secretion of growth factors or enzymes by pancreas tumour cells
?s s4 and lymphotoxin?

14905 S4
120 LYMPHOTOXIN?
S14 0 S4 AND LYMPHOTOXIN?
?s s4 and (migration(w)inhibition(w)factor? or Mif??)

14905 S4
6173 MIGRATION
7974 INHIBITION
53725 FACTOR?
6 MIGRATION(W)INHIBITION(W)FACTOR?
35 MIF??
S15 0 S4 AND (MIGRATION(W)INHIBITION(W)FACTOR? OR MIF??) ?s s4 and (colony(w)stimulating(w)factor? or csf??)

14905 S4
1316 COLONY
10410 STIMULATING
53725 FACTOR?
397 COLONY(W)STIMULATING(W)FACTOR?
841 CSF??
S16 7 S4 AND (COLONY(W)STIMULATING(W)FACTOR? OR CSF??) ?t s16/6/1-7

16/6/1
010281388 WPI Acc No: 95-182646/24
XRAM Acc No: C95-084597
XRPX Acc No: N95-143303
Ink-jet recording sheet with excellent carriage properties - forms at least one ink accepting layer on support and back coated layer(s) hydrated halloysite and silyl denatured PVA on reverse.

16/6/2
010048952 WPI Acc No: 94-316663/39
XRAM Acc No: C94-144254
Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. interleukin, has reduced toxic side effects, useful in vaccines and for treating cancer or immune disease

16/6/3
009520786 WPI Acc No: 93-214328/26
XRAM Acc No: C93-095143

XRPX Acc No: N93-164701
Detection of analytes, eg. bladder tumour analytes, in biological fluids - usign agglutination assays with ***colloidal*** dye and latex particle suspensions

16/6/4
008825351 WPI Acc No: 91-329364/45
XRAM Acc No: C91-142472
Mfg. paper having improved retention of fillers and fines - by adding amphoteric starch and ***colloidal*** silica, bentonite or zeolite as anionic aid to pulp contg. fillers

16/6/5
007431204 WPI Acc No: 88-065139/10
XRAM Acc No: C88-029159
Tumour therapy with monoclonal antibodies or other ligands - which inhibit ***colloidal*** gold pinocytosis or secretion of growth factors or enzymes by pancreas tumour cells

16/6/6
007203413 WPI Acc No: 87-200422/29
XRAM Acc No: C87-083815
Drug delivery system comprises particles of active drug, coated with material which prevents take-up of particles by the liver; ANTI INFECT HYDROPHILIC COAT

16/6/7
004497873 WPI Acc No: 86-001217/01
XRAM Acc No: C86-000445
XRPX Acc No: N86-000930
Staining of proteins and nucleic acids on solid or gel supports by applying suspension of ***colloidal*** metal particles and visualising as coloured signal localised at binding site
?t s16/7/6

16/7/6
DIALOG(R)File 351:DERWENT WPI
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007203413 WPI Acc No: 87-200422/29
XRAM Acc No: C87-083815
Drug delivery system comprises particles of active drug, coated with material which prevents take-up of particles by the liver; ANTI INFECT HYDROPHILIC COAT
Patent Assignee: (COSM-) COSMAS-DAMIAN LTD; (DANB-) DANBIOSYST LTD Author (Inventor): ILLUM L
Number of Patents: 005
Patent Family:

CC Number	Kind	Date	Week	
GB 2185397	A	870722	8729	(Basic)
DE 3700911	A	870723	8730	
GB 2185397	B	891129	8948	
US 4904479	A	900227	9015	
CH 675539	A	901015	9046	

Priority Data (CC No Date): GB 861100 (860117); GB 87851 (870115) Applications (CC,No,Date): DE

3700911 (870114); US 4189 (870115) Abstract (Basic): GB 2185397

Drug delivery system comprises a number of particles of an active drug, each particle coated with a material (I) to form a composite particle which prevents the take up of the composite particle by the liver.

Pref. (I) provides the particles with both a hydrophilic coat that will minimise the uptake of blood components and a steric barrier to particle-cell interaction. Suitable (I) are the block copolymer Tetronic (RTM) 908, a Poloxamer (mixt. of polyoxythylene and polyoxypropylene domains) polymaleic acid or a polymer that is esterified to produce suitable hydrophilic and hydrophobic domains, polysaccharides, hyaluronic acid or xanthan gum.

USE/ADVANTAGE - Drugs administered include anti-infectives (e.g. amphotericin), macrophage activating agents, antithrombotics, cardiovascular agents (e.g. prostaglandins) and anti-leukemia drugs. Particles are directed away from the reticuloendothelial system residing in the liver and spleen. The particles are used to target other sites in the micro-vasculature e.g. subsets in the bone marrow, the liver itself, heart, kidney, lungs and tumour cells if the tumour has a vasculature that allows extravasation. @(15pp Dwg.No 0/10)@ Abstract (US): 9015 US 4904479

New drug delivery system comprise ***colloidal*** suspension of drug with each particle coated and bound with 100-154 Angstroms thickness of hydrophilic material which provides steric barrier to particle-cell interaction. Pref. coating material is polymer which gives both electrostatic and steric barrier, e.g. polyoxypropylene/ polyoxyethylene/ethylenediamine block copolymer contg. 9 units polyoxypropylene and mean 80% wt. polyoxyethylene, known as poloxamine 908. Alternatively pref. coating is

polyoxypropylene/polyoxyethylene/propylene glycol block copolymer contg. 4 units polyoxypropylene and mean 70% wt. polyoxyethylene, known as poloxamer 407. System may be in. particulate form suitable for reconstitution before injection.

USE - For targeting of drugs away from reticuloendothekial system in liver/spleen to other organs, opt. with specific active targetting ligands e.g. monoclonal antibodies, apolipoproteins, sugars, lectins. Useful for immunosuppressants, ***colony*** ***stimulating*** ***factors*** and other peptides, diagnostic radionuclides, antiinfectives and vascular agents. @(13pp)@

Abstract (GB): 8948 GB 2185397

A drug delivery system which, optionally following reconstruction, is suitable for injection as a suspension of ***colloidal*** particles comprising an active drug, each particle being coated with a material which provides a hydrophilic coat of 100-154 Angstroms thickness and a steric to particle-cell interaction.

Derwent Class: A96; B07;

Int Pat Class: A61K-009/14; A61K-045/08; A61K-047/00; A61K-049/00 Derwent Registry Numbers: 1850-U

?s s4 and (vascular(w)endothelial(w)growth(w)factor? or vegf??)

```
        14905  S4
         4349  VASCULAR
          700  ENDOTHELIAL
        43029  GROWTH
        53725  FACTOR?
           10  VASCULAR(W)ENDOTHELIAL(W)GROWTH(W)FACTOR?          14  VEGF??
   S17      0  S4 AND (VASCULAR(W)ENDOTHELIAL(W)GROWTH(W)FACTOR? OR
VEGF??)
```

?s s4 and angiogenin

```
        14905  S4
           30  ANGIOGENIN
   S18      1  S4 AND ANGIOGENIN
```

?t s18/6/1

18/6/1

010048952 WPI Acc No: 94-316663/39

XRAM Acc No: C94-144254

Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. interleukin, has reduced

toxic side effects, useful in vaccines and for treating cancer or immune disease
?s s4 and (heat(w)shock(w)protein? or hsp?)

```
        14905  S4
       452807  HEAT
        33461  SHOCK
        38933  PROTEIN?
           64  HEAT(W)SHOCK(W)PROTEIN?
          105  HSP?
   S19      1  S4 AND (HEAT(W)SHOCK(W)PROTEIN? OR HSP?) ?t s19/6/1
```

19/6/1
010048952 WPI Acc No: 94-316663/39
XRAM Acc No: C94-144254
Compsn. contg. ***colloidal*** metal and immunologically toxic factor - e.g. interleukin, has reduced toxic side effects, useful in vaccines and for treating cancer or immune disease
?s s4 and (blood(w)group?

> > > Unmatched parentheses
?s s4 and (blood(w)group?)

```
        14905  S4
        39601  BLOOD
       149831  GROUP?
          195  BLOOD(W)GROUP?
   S20      0  S4 AND (BLOOD(W)GROUP?)
```

?s s4 and (rh)

```
        14905  S4
         9754  RH
   S21    173  S4 AND (RH)
```

?s s4 and rh(w)factor?

```
        14905  S4
         9754  RH
        53725  FACTOR?
            7  RH(W)FACTOR?
   S22      0  S4 AND RH(W)FACTOR?
```

?s s4 and (fibroblast(w)growth(w)factor? or fgf?)

```
        14905  S4
          848  FIBROBLAST
        43029  GROWTH
        53725  FACTOR?
          260  FIBROBLAST(W)GROWTH(W)FACTOR?
          171  FGF?
   S23      1  S4 AND (FIBROBLAST(W)GROWTH(W)FACTOR? OR FGF?) ?t s23/6/1
```

23/6/1
007431204 WPI Acc No: 88-065139/10
XRAM Acc No: C88-029159
Tumour therapy with monoclonal antibodies or other ligands - which inhibit ***colloidal*** gold

Set Items Description
S1 14468 COLLOID?
S2 53189 COLLOID? OR METAL OR GOLD
S3 13 S2 AND LIPID(W)A
S4 13 RD (unique items)
S5 102 S2 AND INTERFERON?
S6 46 S2 AND INTERFERON?/TI
S7 19 COLLOID? AND INTERFERON?
S8 184 S2 AND PHOSPHOLIPASE?
S9 87 S2 AND PHOSPHOLIPASE?/TI
S10 91161 COLLOID? OR METAL? OR GOLD?
S11 123 S10 AND PHOSPHOLIPASE?/TI
S12 141 S10 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI S13 31787 (COLLOID? OR METAL? OR GOLD?)/TI
S14 39 S13 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI S15 7 S10 AND ENTEROTOXIN(W)B
S16 233 S10 AND INTERFERON?
S17 648 S10 AND INTERLEUKIN?
S18 238 S10 AND INTERLEUKIN?/TI
S19 72 S13 AND INTERLEUKIN?/TI
S20 219 S10 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF) S21 17 S13 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF)/TI S22 50 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF? ??) S23 50 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF??) S24 11 S10 AND LYMPHOTOXIN?
S25 11 S10 AND ((MIGRATION(W)INHIBITION(W)FACTOR) OR MIF) S26 184 S10 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF) S27 12 S13 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF)/TI S28 5 S10 AND ((VASUCLAR(W)EPITHELIAL(W)GROWTH(W)FACTOR) OR VEGF) S29 5 S10 AND ((VASCULAR(W)EPITHELIAL(W)GROWTH(W)FACTOR) OR VEGF) S30 7 S10 AND ((VASCULAR(W)ENDOTHELIAL(W)GROWTH(W)FACTOR) OR VEG- F)
S31 145 "ANGIOGENIN"
S32 96 ANGIOGENIN/TI
S33 3 S10 AND ANGIOGENIN
S34 215 S10 AND ((TRANSFORMING(W)GROWTH(W)FACTOR?) OR TGF??) S35 21 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR?) OR TGF??)/TI S36 201 S10 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?) S37 14 S13 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?)/TI S38 14 S13 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?)/TI S39 87 S10 AND ((FIBROBLAST(W)GROWTH(W)FACTOR?) OR FGF??) S40 5 S13 AND ((FIBROBLAST(W)GROWTH(W)FACTOR?) OR FGF??)/TI S41 25493 BLOOD(W)GROUP?
S42 14 S10 AND (BLOOD(W)GROUP?)/TI
S43 1 S10 AND (ABO)/TI
S44 115 S13 AND (RH OR RH(W)FACTORS?)
S45 33 S10 AND (RH OR RH(W)FACTORS?)/TI
S46 11 (COLLOID?/TI AND TOXIC?/TI)

File 155:MEDLINE(R) 1966-1995/Aug W4
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Set Items Description
--- ----- -----------
?s colloid?

S1 14468 COLLOID?
?s s1 and lipid(w)A

Processing

?s colloid? or metal or gold

14468 COLLOID?
24735 METAL
18213 GOLD
S2 53189 COLLOID? OR METAL OR GOLD
?s s2 and lipid(w)A

Processing
Processing
53189 S2
84697 LIPID
4039508 A
2093 LIPID(W)A
S3 13 S2 AND LIPID(W)A
?rd

...completed examining records
S4 13 RD (unique items)
?t s4/6/1-13

?t s4/7/11

4/7/11
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1995 Knight-Ridder Info. All rts. reserv.

02854881 76035881
Physical state and biological activity of lipopolysaccharides. Toxicity and immunogenicity of the ***lipid*** ***A*** component.
Galanos C
Z Immunitatsforsch Exp Klin Immunol (GERMANY, WEST) Jul 1975, 149 (2-4) p214-29, ISSN 0300-872X Journal Code: XW2
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Bacterial lipopolysaccharides are negatively charged macromolecules due to the presence of phosphate, pyrophosphate and carboxyl groups. When isolated from bacteria, they are obtained in salt form with ***metal*** cations and basic amines. Removal of these ionically bound substances by electrodialysis leads to acidic lipopolysaccharides which on neutralizing with different bases, preparations are obtained which

show distinct differences in their physico-chemical properties and in their biological activity. Soluble lipopolysaccharides interact with complement leading to loss of hemolytic activity. This property is embedded in the ***lipid*** ***A*** part of the molecule and is expressed only when the lipopolysaccharide is present in a favourable particle size. Nevertheless, a number of lipopolysaccharides exists, which, regardless of their particle size do not interact with complement. ***Lipid*** ***A*** is the part of the molecule responsible for endotoxicity. This was demonstrated by employing solubilized ***lipid*** ***A*** in complex form with BSA. Soluble ***lipid*** ***A*** /BSA complexes proved highly toxic for mice and pyrogenic in rabbits, and express many biological activities exhibited by intact lipopolysaccharides. ***Lipid*** ***A*** , when exposed on the bacterial cell-surface acts as a powerful immunogen, giving rise to the production of specific anti-***lipid*** ***A*** antibodies that interact with the ***lipid*** ***A*** obtained from lipopolysaccharides that are otherwise distinct in their O-serological specificity. Anti-***lipid*** ***A*** antibodies occur naturally in the serum of many animals and humans. The biological significance of anti-***lipid*** ***A*** antibodies is discussed.
?display sets

Set Items Description
S1 14468 COLLOID?
S2 53189 COLLOID? OR METAL OR GOLD
S3 13 S2 AND LIPID(W)A
S4 13 RD (unique items)
?s s2 and interferon?

53189 S2
38648 INTERFERON?
S5 102 S2 AND INTERFERON?
?s s2 and interferon?/ti

53189 S2
20677 INTERFERON?/TI
S6 46 S2 AND INTERFERON?/TI
?t s6/6/1-46

?s colloid? and interferon?

14468 COLLOID?
38648 INTERFERON?
S7 19 COLLOID? AND INTERFERON?
?s s7/6/1-19

>>>Invalid syntax
?t s7/6/1-19

7/7/4
DIALOG(R)File 155:MEDLINE(R)
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07445493 90352493
A phase I study of recombinant human interleukin-2 and alpha- ***interferon*** -2a in patients with renal cell cancer, colorectal cancer, and malignant melanoma.

Mittelman A; Huberman M; Puccio C; Fallon B; Tessitore J; Savona S; Eyre R; Gafney E; Wick M; Skelos A; et al

New York Medical College, Valhalla 10595.

Cancer (UNITED STATES) Aug 15 1990, 66 (4) p664-9, ISSN 0008-543X Journal Code: CLZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Preclinical data suggest synergy of interleukin-2 (IL-2) combined with alpha-***interferon*** (IFN). In addition, toxicities of IL-2 may be decreased by intermittent continuous infusion. The purpose of this trial was to determine the maximum tolerated dose (MTD) of recombinant IL-2 combined with alpha-IFN in patients with renal cancer, colon cancer, melanoma, and malignant B-cell disease. IL-2 was given by continuous i.v. infusion at an initial dose of 5 X 10(5) units (U)/m2/d for 4 days plus IFN at 6 X 10(6) U/m2/d intramuscularly days 1 and 4 weekly for 4 weeks. Patients who achieved a response or stable disease received an additional 4 weeks of therapy. IL-2 doses were increased to 1, 2, 3, 5, and 7 X 10(6) U/m2/d with three to eight patients at each dose level, at each of the two participating institutions. The dose of IFN was 6 X 10(6) U/m2 days 1 and 4 for all but five patients whose IFN dose was doubled to 12 X 10(6) U/m2/d. Forty-three patients were entered on this study with 34 completing at least 4 weeks of therapy. Six patients were taken off study because of Grades III or IV pulmonary, neurologic, or cardiac toxicity; one for progressive disease; one for CNS metastases, and one for personal reasons. All of the toxicities were reversible. Chills and fever were universal, especially on days 1 and 4. Mild and moderate nausea, vomiting, diarrhea, anorexia, malaise, and cutaneous erythema were present in most patients. Fluid retention and occasional pleural effusions were observed at the higher IL-2 doses but were not dose-limiting. Significant hypotension associated with oliguria was seen, and these patients were treated with vasopressors and ***colloids*** . None of the patients required ICU admission. Thirty-four patients were evaluable for response. There were 4/18 (22%) renal cell patients who experienced a partial response. No responses were seen in patients with melanoma, lymphoma, or colorectal cancer. The combined debilitating symptoms of fatigue, diarrhea, hypotension, fluid retention, and anorexia defined the MTD as 5 X 10(6) U/m2/d of IL-2 and 6 X 10(6) U/m2 of alpha-IFN.

?display sets

Set	Items	Description
S1	14468	COLLOID?
S2	53189	COLLOID? OR METAL OR GOLD
S3	13	S2 AND LIPID(W)A
S4	13	RD (unique items)
S5	102	S2 AND INTERFERON?
S6	46	S2 AND INTERFERON?/TI
S7	19	COLLOID? AND INTERFERON?

?s s2 and phospholipase?

	53189	S2
	19495	PHOSPHOLIPASE?
S8	184	S2 AND PHOSPHOLIPASE?

?s s2 and phospholipase?/ti

	53189	S2
	6949	PHOSPHOLIPASE?/TI
S9	87	S2 AND PHOSPHOLIPASE?/TI

?s colloid? or metal? or gold?

	14468	COLLOID?
	51619	METAL?
	29899	GOLD?
S10	91161	COLLOID? OR METAL? OR GOLD?

?s s10 and phospholipase?/ti

```
        91161  S10
         6949  PHOSPHOLIPASE?/TI
   S11    123  S10 AND PHOSPHOLIPASE?/TI
```

?t s11/6/1-123

?t s11/7/23,61

11/7/23
DIALOG(R)File 155:MEDLINE(R)
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08222071 92360071
Inhibition of human ***phospholipase*** C by aurothiomalate and (triethylphosphine) ***gold*** complexes.
Marki F; Stanton JL
Research Department, Ciba-Geigy Ltd., Basel, Switzerland. Arzneimittelforschung (GERMANY) Mar 1992, 42 (3) p328-33, ISSN 0004-4172 Journal Code: 91U
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The effect of several ***gold*** complexes on the activity of phospholipase C from human blood platelets was studied in vitro. Aurothiomalate and auranofin--2 agents used for the chrysotherapy of rheumatoid arthritis--, ***gold*** chloride, (triethylphosphine)***gold*** chloride, and 5 newly synthesized (triethylphosphine)***gold*** complexes dose-dependently inhibited the enzyme with IC50 values between 0.8 mumol/l ((triethylphosphine)***gold*** chloride) and over 100 mumol/l (auranofin). None of the compounds affected phospholipase A2 from human polymorphonuclear leukocytes at concentrations up to 100 mumol/l. Inhibition of phospholipase C by (triethylphosphine)***gold*** chloride, aurothiomalate, and compound 3 was not significantly different at substrate concentrations of 20 and 100 mumol/l phosphatidylinositol, suggesting that these ***gold*** complexes do not inhibit phospholipase C by competing with the substrate. After confirming the Ca2+ dependence of the human platelet phospholipase C by demonstrating inhibition by the Ca2+ chelators EDTA and EGTA--but no inhibition by the Zn2+ chelator 1,10-phenanthroline--the inhibition of the enzyme by (triethylphosphine)***gold*** chloride, aurothiomalate, and compound 3 was studied at 3 different concentrations of Ca2+ in the range of 0.2 to 2 mmol/l. Inhibition by (triethylphosphine) ***gold*** chloride was not affected by changes of Ca2+, whereas inhibition by aurothiomalate and compound 3 was markedly suppressed by increasing the Ca2+ concentration.(ABSTRACT TRUNCATED AT 250 WORDS)

11/7/61
DIALOG(R)File 155:MEDLINE(R)
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06393766 88038766
Effect of auranofin and other ***gold*** complexes on the activity of ***phospholipase*** C.
Snyder RM; Mirabelli CK; Clark MA; Ziegler JT; Crooke ST Department of Molecular Pharmacology, Smith Kline & French Laboratories, Philadelphia, Pennsylvania 19101.
Mol Pharmacol (UNITED STATES) Sep 1987, 32 (3) p437-42, ISSN 0026-895X Journal Code: NGR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Auranofin (AF) is an orally active chrysotherapeutic agent used for the treatment of rheumatoid arthritis,

a self-perpetuating inflammatory disease. Because of reports suggesting that AF and other ***gold*** complexes can, under certain circumstances, exacerbate rheumatoid inflammatory lesions in humans and adjuvant arthritic rats and that phospholipase C (PLC) and phospholipase A2 activities are increased in rheumatoid patients, the effects of AF and a related ***gold*** complex on in situ mammalian and purified Bacillus cereus PLC were examined. Results of our studies show that 1) AF and triethylphosphine ***gold*** chloride (TEPG), an AF analog, stimulated PLC activity in the sonicate of RAW 264.7 macrophages; 2) AF and TEPG stimulated B. cereus PLC activity in a concentration-dependent manner, but the pattern of stimulation and concentrations of drugs required to stimulate the purified enzyme differ from those seen with the macrophage PLC; 3) ***metals*** (cobalt and zinc) and sulfhydryl reagents (N-ethylmaleimide, iodoacetic acid, and glutathione), tested at the same concentrations of AF that enhanced PLC activity, had no effect on the enzyme. These data suggest that stimulation of PLC may be a generic phenomenon since two divergent PLCs are affected by ***gold*** complexes. Additionally, these studies may provide one potential explanation for rheumatoid lesion flares seen in patients and animals on chrysotherapy.
?display sets

Set	Items	Description
S1	14468	COLLOID?
S2	53189	COLLOID? OR METAL OR GOLD
S3	13	S2 AND LIPID(W)A
S4	13	RD (unique items)
S5	102	S2 AND INTERFERON?
S6	46	S2 AND INTERFERON?/TI
S7	19	COLLOID? AND INTERFERON?
S8	184	S2 AND PHOSPHOLIPASE?
S9	87	S2 AND PHOSPHOLIPASE?/TI
S10	91161	COLLOID? OR METAL? OR GOLD?
S11	123	S10 AND PHOSPHOLIPASE?/TI

?s s10 and (endotoxin? or lipopolysaccharide? or lps)/ti

	91161	S10
	7648	ENDOTOXIN?/TI
	5438	LIPOPOLYSACCHARIDE?/TI
	749	LPS/TI
S12	141	S10 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI ?t s12/6/1-50

?s (colloid? or metal? or gold?)/ti

	3283	COLLOID?/TI
	18004	METAL?/TI
	11076	GOLD?/TI
S13	31787	(COLLOID? OR METAL? OR GOLD?)/TI

?s s13 and (endotoxin? or lipopolysaccharide? or lps)/ti

	31787	S13
	7648	ENDOTOXIN?/TI
	5438	LIPOPOLYSACCHARIDE?/TI
	749	LPS/TI
S14	39	S13 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI ?t s14/6/1-39

?s s10 and enterotoxin(w)B

91161 S10
4714 ENTEROTOXIN
302760 B
736 ENTEROTOXIN(W)B
S15 7 S10 AND ENTEROTOXIN(W)B
?t s15/6/7

?s s10 and interferon?

91161 S10
38648 INTERFERON?
S16 233 S10 AND INTERFERON?
?s s10 and interleukin?

91161 S10
48072 INTERLEUKIN?
S17 648 S10 AND INTERLEUKIN?
?s s10 and interleukin?/ti

91161 S10
17772 INTERLEUKIN?/TI
S18 238 S10 AND INTERLEUKIN?/TI
?s s13 and interleukin?/ti

31787 S13
17772 INTERLEUKIN?/TI
S19 72 S13 AND INTERLEUKIN?/TI
?t s19/6/1-72

19/7/2
DIALOG(R)File 155:MEDLINE(R)
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09336100 95266100
Lung toxicity of hard ***metal*** particles and production of ***interleukin*** -1, tumor necrosis factor-alpha, fibronectin, and cystatin-c by lung phagocytes.
Huaux F; Lasfargues G; Lauwerys R; Lison D
Industrial Toxicology and Occupational Medicine Unit, School of Medicine, Catholic University of Louvain, Brussels, Belgium.
Toxicol Appl Pharmacol (UNITED STATES) May 1995, 132 (1) p53-62, ISSN 0041-008X Journal Code: VWO
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Hard metal alloys (WC-Co) are made of a mixture of cobalt (Co; 6%) and tungsten carbide (WC; 94%) particles. Chronic inhalation of hard metal dust can lead to the development of a fibrosing alveolitis, the pathogenesis of which is still undefined. The present investigation was undertaken to assess the effect of Co, WC, and WC-Co particles on the release by lung phagocytes of interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-alpha), fibronectin, and cystatin-c. The responses were compared with those induced by two other lung toxicants, i.e., crystalline silica (DQ12) and arsenic trioxide (As2O3). IL-1 and TNF-alpha

activities produced in the presence and absence of LPS stimulation were measured with the aid of bioassays while fibronectin and cystatin-c were determined by latex immunoassays. In vitro, maximal noncytotoxic doses of As2O3, Co, WC, or WC-Co did not significantly affect the production of these mediators by rat alveolar macrophages. In contrast, DQ12 enhanced the production of TNF-alpha (with and without LPS stimulation) and IL-1 (after LPS stimulation) and decreased cystatin-c release (in the absence of LPS). Following a single intratracheal instillation of the different test preparations in the rat, the response of the lung phagocytes obtained by bronchoalveolar lavage (BAL) 24 hr later was examined. We were unable to detect any consistent effect of Co (0.06 mg/100 g body wt), WC (1 mg/100 g body wt), or WC-Co treatment (1 mg/100 g body wt) on the production of the above mediators. In contrast, after LPS stimulation, As2O3 (0.5 mg/100 g body wt) and DQ12 (1 mg/100 g body wt) stimulated the production of TNF-alpha and IL-1. In the absence of LPS, As2O3 stimulated fibronectin and cystatin-c production and DQ12 stimulated cystatin-c release. Since the dose of WC-Co used in vivo (1 mg/100 g body wt) caused pronounced lung inflammation (increased LDH, protein, and albumin levels in BAL fluid), we conclude that the acute lung toxicity of WC-Co particles is not mediated through enhanced production of the examined mediators by lung phagocytes.

19/7/27
DIALOG(R)File 155:MEDLINE(R)
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08557519 93267519
Gold therapy lowers serum ***interleukin*** 6 levels in rheumatoid arthritis.
Madhok R; Crilly A; Murphy E; Smith J; Watson J; Capell HA Centre for Rheumatic Diseases, Glasgow Royal Infirmary, Glasgow, Scotland, UK.
J Rheumatol (CANADA) Apr 1993, 20 (4) p630-3, ISSN 0315-162X Journal Code: JWX
Languages: ENGLISH
Document type: JOURNAL ARTICLE
OBJECTIVE. To determine the clinical utility and the effect of sodium aurothiomalate (GSTM) on serum interleukin 6 (IL-6) levels in patients with rheumatoid arthritis (RA). METHODS. Open prospective study of 50 patients with RA treated with GSTM. Serum IL-6 measured by bioassay. RESULTS. IL-6 showed correlations with Ritchie articular index, duration of morning stiffness and C-reactive protein. GSTM significantly reduced IL-6 levels. CONCLUSIONS. IL-6 is a potentially useful additional indicator of disease activity in RA and is modulated by GSTM.

19/7/31
DIALOG(R)File 155:MEDLINE(R)
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08485239 93195239
Effect of ***metals*** on ***interleukin*** -6 (IL-6) mitogenic stimulation of murine hybridoma cells.
Orupabo I; Hay A; Evans SW
Department of Clinical Medicine, Old Medical School, University of Leeds, United Kingdom.
Immunopharmacol Immunotoxicol (UNITED STATES) 1992, 14 (4) p723-36, ISSN 0892-3973 Journal Code: IAI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The effect of several divalent metal cations (Co, Cu, Zn, Hg and Pb) on the proliferative response of B9 hybridoma cells to IL-6 has been investigated. At concentrations which are not cytotoxic all the metals inhibited proliferation. The inhibition by Cd and Pb was dependent on both time of addition of the metal and IL-6 concentration. Cd (10 microM) and Pb (50 microM) added at the same time as IL-6 were inhibitory but added 24h later had no effect. Increasing the concentration of IL-6 overcame the inhibitory effect of Cd (10 microM) and Pb (50 microM). Inhibition caused by the other metals was independent of either time of

addition or IL-6 concentration. IL-6 did not stimulate an increased intracellular concentration of metallothionein suggesting that the protective effect of IL-6 is not mediated via induction of metallothionein. The results suggest that there are at least two distinct metal sensitive events in B9 proliferation, i) IL-6 reversible inhibition by Cd and Pb ii) IL-6 independent inhibition by Co, Cu and Hg.

19/7/68
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06496179 88141179
Effects of ***gold*** on the production of and response to human ***interleukin***-1.
Drakes ML; Harth M; Galsworthy SB; McCain GA
Department of Microbiology and Immunology, University of Western Ontario, London, Canada.
J Rheumatol (CANADA) Dec 1987, 14 (6) p1123-7, ISSN 0315-162X Journal Code: JWX
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We studied the effects in vitro of sodium aurothiomalate (GSTM) on the production of, and response to, a monocyte supernatant with interleukin-1 (IL-1)-like activity. Monocyte supernatant was produced by human peripheral blood monocytes stimulated with lipoprotein polysaccharide, and its IL-1-like activity assayed by its effect on tritiated thymidine incorporation by C3H/HeJ mouse thymocytes. GSTM inhibited the thymocyte response to monocyte supernatant even when added to monocyte supernatant and thymocytes after 48 h of culture. GSTM also inhibited production of IL-1-like activity by monocytes, when added to culture within the first 22 h. Inhibition of both response to and production of monocyte supernatant was dose dependent. These effects of GSTM on Il-1-like activity may constitute one of the mechanisms of action of the drug in rheumatoid arthritis.
?s s10 and ((tumor(w)necrosis(w)factor) or TNF)

```
      91161 S10
     252028 TUMOR
      67267 NECROSIS
     269305 FACTOR
      16008 TUMOR(W)NECROSIS(W)FACTOR
      12062 TNF
S20     219 S10 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF) ?s s13 and
((tumor(w)necrosis(w)factor) or TNF)/ti

      31787 S13
      65044 TUMOR/TI
      14735 NECROSIS/TI
      87181 FACTOR/TI
       5470 TUMOR/TI(W)NECROSIS/TI(W)FACTOR/TI
       1662 TNF/TI
S21      17 S13 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF)/TI ?t s21/6/1-17
```

?s s13 and ((transforming(w)growth(w)factor) or TGF? ??)

```
      31787 S13
      16178 TRANSFORMING
     376582 GROWTH
     269305 FACTOR
       7658 TRANSFORMING(W)GROWTH(W)FACTOR
       6441 TGF? ??
S22      50 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF? ??) ?s s13 and
```

((transforming(w)growth(w)factor) or TGF??)

```
        31787  S13
        16178  TRANSFORMING
       376582  GROWTH
       269305  FACTOR
         7658  TRANSFORMING(W)GROWTH(W)FACTOR
         6454  TGF??
   S23     50  S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF??) ?t s23/6/1-50
```

?s s10 and lymphotoxin?

```
        91161  S10
         1537  LYMPHOTOXIN?
   S24     11  S10 AND LYMPHOTOXIN?
```

?t s24/6/1-11

?s s10 and ((migration(w)inhibition(w)factor or MIF)

> > > Unmatched parentheses
?s s10 and ((migration(w)inhibition(w)factor) or MIF)

```
        91161  S10
        30292  MIGRATION
       219166  INHIBITION
       269305  FACTOR
          461  MIGRATION(W)INHIBITION(W)FACTOR
         1168  MIF
   S25     11  S10 AND ((MIGRATION(W)INHIBITION(W)FACTOR) OR MIF) ?t s25/6/1-11
```

?t s25/7/7

25/7/7
DIALOG(R)File 155:MEDLINE(R)
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04152752 80263752
Pneumonitis caused by ***gold*** salt therapy: evidence for the role of cell-mediated immunity in its pathogenesis.
McCormick J; Cole S; Lahirir B; Knauft F; Cohen S; Yoshida T Am Rev Respir Dis (UNITED STATES) Jul 1980, 122 (1) p145-52, ISSN 0003-0805 Journal Code: 426
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Gold salt-related pneumonitis is now an established clinical entity, but the mechanism for the induction of the pulmonary disease is not known. In 2 patients with this disorder, we observed elaboration of the lymphokines, ***migration*** ***inhibition*** ***factor*** (***MIF***) and macrophage chemotactic factor (MCF), by peripheral blood lymphocytes after incubation with ***gold*** salt. Incorporation of [3H]thymidine was not seen with several different dosages of ***gold*** salt. Control lymphocytes from normal subjects, from patients with rheumatoid arthritis but not receiving ***gold*** salt, and from patients with rheumatoid arthritis receiving ***gold*** salt but without hypersensitivity manifestations, were all

unresponsive to the drug. These results suggested that the pneumonitis associated with chrysotherapy is also associated with a specific cellular immune response to the drug. Further, they point to the necessity of evaluating multiple parameters of cellular immunity, because in these patients there was a dissociation between blast transformation and mediator production. In addition, they underscored the need for further observations of cellular responsiveness in patients receiving ***gold*** salt therapy with and without overt pulmonary disease.
?s s10 and ((colony(w)stimulating(w)factor?) or csf)

```
        91161  S10
        36199  COLONY
        46676  STIMULATING
      1144555  FACTOR?
        12234  COLONY(W)STIMULATING(W)FACTOR?
        23752  CSF
   S26    184  S10 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF) ?s s13 and
((colony(w)stimulating(w)factor?) or csf)/ti

        31787  S13
         8299  COLONY/TI
        12011  STIMULATING/TI
       154705  FACTOR?/TI
         4108  COLONY/TI(W)STIMULATING/TI(W)FACTOR?/TI
         4838  CSF/TI
   S27     12  S13 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF)/TI ?t s27/6/1-12


?t s27/7/12


 27/7/12
DIALOG(R)File 155:MEDLINE(R)
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00041680   66041680
  The effect of ***CSF*** paraproteins on the ***colloidal*** ***gold*** test.
  Weiss AH; Christoff N
  Arch Neurol (UNITED STATES)  Jan 1966,  14 (1) p100-6,  ISSN 0003-9942 Journal Code: 80K
  Languages: ENGLISH
  Document type: JOURNAL ARTICLE
?display sets


Set    Items  Description
S1     14468  COLLOID?
S2     53189  COLLOID? OR METAL OR GOLD
S3        13  S2 AND LIPID(W)A
S4        13  RD (unique items)
S5       102  S2 AND INTERFERON?
S6        46  S2 AND INTERFERON?/TI
S7        19  COLLOID? AND INTERFERON?
S8       184  S2 AND PHOSPHOLIPASE?
S9        87  S2 AND PHOSPHOLIPASE?/TI
S10    91161  COLLOID? OR METAL? OR GOLD?
S11      123  S10 AND PHOSPHOLIPASE?/TI
```

S12 141 S10 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI S13 31787 (COLLOID? OR METAL? OR GOLD?)/TI
S14 39 S13 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI S15 7 S10 AND ENTEROTOXIN(W)B
S16 233 S10 AND INTERFERON?
S17 648 S10 AND INTERLEUKIN?
S18 238 S10 AND INTERLEUKIN?/TI
S19 72 S13 AND INTERLEUKIN?/TI
S20 219 S10 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF) S21 17 S13 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF)/TI S22 50 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF? ??) S23 50 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF??) S24 11 S10 AND LYMPHOTOXIN?
S25 11 S10 AND ((MIGRATION(W)INHIBITION(W)FACTOR) OR MIF) S26 184 S10 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF) S27 12 S13 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF)/TI ?s s10 and ((vasuclar(w)epithelial(w)growth(w)factor or vegf)
> > > Unmatched parentheses
?s s10 and ((vasuclar(w)epithelial(w)growth(w)factor) or vegf)
91161 S10
6 VASUCLAR
62203 EPITHELIAL
376582 GROWTH
269305 FACTOR
0 VASUCLAR(W)EPITHELIAL(W)GROWTH(W)FACTOR
191 VEGF
S28 5 S10 AND ((VASUCLAR(W)EPITHELIAL(W)GROWTH(W)FACTOR) OR VEGF)
?s s10 and ((vascular(w)epithelial(w)growth(w)factor) or vegf)
91161 S10
166921 VASCULAR
62203 EPITHELIAL
376582 GROWTH
269305 FACTOR
0 VASCULAR(W)EPITHELIAL(W)GROWTH(W)FACTOR
191 VEGF
S29 5 S10 AND ((VASCULAR(W)EPITHELIAL(W)GROWTH(W)FACTOR) OR VEGF)
?t s29/6/1-5

29/6/1
09316275 95246275
Regulation of vascular endothelial growth factor in cardiac myocytes.

29/6/2
09175266 95105266
Purification and characterization of two collagenase inhibitors from mouse sarcoma 180 conditioned medium.

29/6/3
09032782 94347782
Inhibition of receptor binding by high-affinity RNA ligands to vascular endothelial growth factor.

29/6/4
08367709 93077709
Vascular endothelial growth factor induces interstitial collagenase expression in human endothelial cells.

29/6/5
07906324 92044324
Distribution of vascular permeability factor (vascular endothelial growth factor) in tumors: concentration in tumor blood vessels.
?s s10 and ((vascular(w)endothelial(w)growth(w)factor) or vegf)
91161 S10
166921 VASCULAR
36635 ENDOTHELIAL
376582 GROWTH
269305 FACTOR
227 VASCULAR(W)ENDOTHELIAL(W)GROWTH(W)FACTOR
191 VEGF
S30 7 S10 AND ((VASCULAR(W)ENDOTHELIAL(W)GROWTH(W)FACTOR) OR VEGF)
?t s30/6/1-7

30/6/1
09316275 95246275
Regulation of ***vascular*** ***endothelial*** ***growth*** ***factor*** in cardiac myocytes.

30/6/2
09175266 95105266
Purification and characterization of two collagenase inhibitors from mouse sarcoma 180 conditioned medium.

30/6/3
09032782 94347782
Inhibition of receptor binding by high-affinity RNA ligands to ***vascular*** ***endothelial*** ***growth*** ***factor***.

30/6/4
08944791 94259791
Cellular markers that distinguish the phases of hemangioma during infancy and childhood.

30/6/5
08367709 93077709
Vascular ***endothelial*** ***growth*** ***factor*** induces interstitial collagenase expression in human endothelial cells.

30/6/6
08308865 93018865
Expression of vascular permeability factor (***vascular*** ***endothelial*** ***growth*** ***factor***) by epidermal keratinocytes during wound healing.

30/6/7

07906324 92044324
Distribution of vascular permeability factor (***vascular*** ***endothelial*** ***growth*** ***factor***) in tumors: concentration in tumor blood vessels.
?e antiogenin

Ref	Items	Index-term
E1	2	ANTIOFIDICOS
E2	1	ANTIOFLOGISTICO
E3	0	*ANTIOGENIN
E4	3	ANTIOGENSIN
E5	1	ANTIOGONADOTROPIN
E6	1	ANTIOGRAFII
E7	6	ANTIOGRAPHIC
E8	8	ANTIOGRAPHY
E9	1	ANTIOGUENA
E10	1	ANTIOGUIA
E11	1	ANTIOHIDANTS
E12	1	ANTIOKHOLINESTERAZNUIU

Enter P or PAGE for more
?e angiogenin

Ref	Items	Index-term
E1	5	ANGIOGENICITY
E2	1	ANGIOGENICO
E3	145	*ANGIOGENIN
E4	1	ANGIOGENIN, METHIONYL-(-1)-
E5	6	ANGIOGENINA
E6	4	ANGIOGENINS
E7	3	ANGIOGENIQUE
E8	1	ANGIOGENIQUES
E9	2	ANGIOGENNA
E10	1	ANGIOGENNE
E11	1	ANGIOGENNNOGO
E12	4	ANGIOGENNOGO

Enter P or PAGE for more
?s e3

S31 145 "ANGIOGENIN"
?s angiogenin/ti

S32 96 ANGIOGENIN/TI
?t s32/6/1-5

32/6/1
09294057 95224057
Crystal structure of bovine ***angiogenin*** at 1.5-A resolution.

32/6/2
09287323 95217323

A comparison of the predicted and X-ray structures of ***angiogenin***. Implications for further studies of model building of homologous proteins.

32/6/3
09249301 95179301
The effect of ***angiogenin*** on blood vessel proliferation in rats] Vliianie angiogenina na proliferatsiiu krovenosnykh sosudov u krys.

32/6/4
09202615 95132615
Angiogenin antagonists prevent tumor growth in vivo.

32/6/5
09164806 95094806
The widespread expression of ***angiogenin*** in different human cells suggests a biological function not only related to angiogenesis. ?s s10 and angiogenin

91161 S10
145 ANGIOGENIN
S33 3 S10 AND ANGIOGENIN
?t s33/6/1-3

33/6/1
07049584 89351584
Conformational characterization of human ***angiogenin*** by limited proteolysis.

33/6/2
06971623 89273623
Characterization of ribonucleolytic activity of ***angiogenin*** towards tRNA.

33/6/3
06816254 89118254
Expression of human ***angiogenin*** in cultured baby hamster kidney cells.
?s s10 and ((transforming(w)growth(w)factor?) or tgf??)

91161 S10
16178 TRANSFORMING
376582 GROWTH
1144555 FACTOR?
8267 TRANSFORMING(W)GROWTH(W)FACTOR?
6454 TGF??
S34 215 S10 AND ((TRANSFORMING(W)GROWTH(W)FACTOR?) OR TGF??) ?s s13 and ((transforming(w)growth(w)factor?) or tgf??)/ti
31787 S13
5367 TRANSFORMING/TI
96256 GROWTH/TI
154705 FACTOR?/TI
3572 TRANSFORMING/TI(W)GROWTH/TI(W)FACTOR?/TI 1091 TGF??/TI
S35 21 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR?) OR TGF??)/TI ?t s35/6/1-21

91161 S10
78622 HEAT
52368 SHOCK
774553 PROTEIN?
6483 HEAT(W)SHOCK(W)PROTEIN?
4127 HSP?
S36 201 S10 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?) ?s s13 and ((heat(w)shock(w)protein?) or hsp?)/ti

31787 S13
13792 HEAT/TI
21499 SHOCK/TI
208560 PROTEIN?/TI
1730 HEAT/TI(W)SHOCK/TI(W)PROTEIN?/TI
1161 HSP?/TI
S37 14 S13 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?)/TI ?t s37/6/1-14

?s s13 and ((heat(w)shock(w)protein?) or hsp?)/ti

31787 S13
13792 HEAT/TI
21499 SHOCK/TI
208560 PROTEIN?/TI
1730 HEAT/TI(W)SHOCK/TI(W)PROTEIN?/TI
1161 HSP?/TI
S38 14 S13 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?)/TI ?s s10 and ((fibroblast(w)growth(w)factor? or fgf??)

>>>Unmatched parentheses
?s s10 and ((fibroblast(w)growth(w)factor?) or fgf??)

91161 S10
20625 FIBROBLAST
376582 GROWTH
1144555 FACTOR?
5614 FIBROBLAST(W)GROWTH(W)FACTOR?
2251 FGF??
S39 87 S10 AND ((FIBROBLAST(W)GROWTH(W)FACTOR?) OR FGF??) ?s s13 and ((fibroblast(w)growth(w)factor?) or fgf??)/ti

31787 S13
5846 FIBROBLAST/TI
96256 GROWTH/TI
154705 FACTOR?/TI
2166 FIBROBLAST/TI(W)GROWTH/TI(W)FACTOR?/TI
465 FGF??/TI
S40 5 S13 AND ((FIBROBLAST(W)GROWTH(W)FACTOR?) OR FGF??)/TI ?t s40/6/1-5

40/6/1
09307147 95237147
Basic ***fibroblast*** ***growth*** ***factor*** stimulates expression of interstitial collagenase and

inhibitors of ***metalloproteinases*** in rat bone cells.

40/6/2
08858455 94173455
Fibroblast ***growth*** ***factor*** induces proliferating cell nuclear antigen-immunoreactive cells in ***goldfish*** retina.

40/6/3
08209254 92347254
Effect of in vivo administration of recombinant acidic ***fibroblast*** ***growth*** ***factor*** on thyroid function in the rat: induction of ***colloid*** goiter.

40/6/4
07990545 92128545
Differential regulation of ***metalloprotease*** steady-state mRNA levels by IL-1 and ***FGF*** in rabbit articular chondrocytes.

40/6/5
07959735 92097735
Immunolocalization of basic ***fibroblast*** ***growth*** ***factor*** and its receptor in adult ***goldfish*** retina.
?s blood(w)group?

```
      1277620  BLOOD
       640668  GROUP?
   S41   25493  BLOOD(W)GROUP?
```

?s s10 and (blood(w)group?)/ti

```
        91161  S10
       170718  BLOOD/TI
        62474  GROUP?/TI
         5648  BLOOD/TI(W)GROUP?/TI
   S42     14  S10 AND (BLOOD(W)GROUP?)/TI
```

?t s42/6/1-14

?s s10 and (ABO)/ti

```
        91161  S10
         2316  ABO/TI
   S43      1  S10 AND (ABO)/TI
```

?t s43/6/1

43/6/1
06719415 89021415
Immunocytochemical study on the ultrastructural localization of human-type ***ABO*** (H)-blood group activities in a macaque (Macaca irus). ?s s13 and (Rh or Rh(w)factors?)

```
        31787  S13
        71438  RH
```

71438 RH
958715 FACTORS?
32 RH(W)FACTORS?
S44 115 S13 AND (RH OR RH(W)FACTORS?)
?s s10 and (Rh or Rh(w)factors?)/ti

91161 S10
4176 RH/TI
4176 RH/TI
66711 FACTORS?/TI
26 RH/TI(W)FACTORS?/TI
S45 33 S10 AND (RH OR RH(W)FACTORS?)/TI
?t s45/6/1-33

?display sets

Set Items Description
S1 14468 COLLOID?
S2 53189 COLLOID? OR METAL OR GOLD
S3 13 S2 AND LIPID(W)A
S4 13 RD (unique items)
S5 102 S2 AND INTERFERON?
S6 46 S2 AND INTERFERON?/TI
S7 19 COLLOID? AND INTERFERON?
S8 184 S2 AND PHOSPHOLIPASE?
S9 87 S2 AND PHOSPHOLIPASE?/TI
S10 91161 COLLOID? OR METAL? OR GOLD?
S11 123 S10 AND PHOSPHOLIPASE?/TI
S12 141 S10 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI S13 31787 (COLLOID? OR METAL? OR GOLD?)/TI
S14 39 S13 AND (ENDOTOXIN? OR LIPOPOLYSACCHARIDE? OR LPS)/TI S15 7 S10 AND ENTEROTOXIN(W)B
S16 233 S10 AND INTERFERON?
S17 648 S10 AND INTERLEUKIN?
S18 238 S10 AND INTERLEUKIN?/TI
S19 72 S13 AND INTERLEUKIN?/TI
S20 219 S10 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF) S21 17 S13 AND ((TUMOR(W)NECROSIS(W)FACTOR) OR TNF)/TI S22 50 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF? ??) S23 50 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR) OR TGF??) S24 11 S10 AND LYMPHOTOXIN?
S25 11 S10 AND ((MIGRATION(W)INHIBITION(W)FACTOR) OR MIF) S26 184 S10 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF) S27 12 S13 AND ((COLONY(W)STIMULATING(W)FACTOR?) OR CSF)/TI S28 5 S10 AND ((VASUCLAR(W)EPITHELIAL(W)GROWTH(W)FACTOR) OR VEGF) S29 5 S10 AND ((VASCULAR(W)EPITHELIAL(W)GROWTH(W)FACTOR) OR VEGF) S30 7 S10 AND ((VASCULAR(W)ENDOTHELIAL(W)GROWTH(W)FACTOR) OR VEG- F)
S31 145 "ANGIOGENIN"
S32 96 ANGIOGENIN/TI
S33 3 S10 AND ANGIOGENIN
S34 215 S10 AND ((TRANSFORMING(W)GROWTH(W)FACTOR?) OR TGF??) S35 21 S13 AND ((TRANSFORMING(W)GROWTH(W)FACTOR?) OR TGF??)/TI S36 201 S10 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?) S37 14 S13 AND ((HEAT(W)SHOCK(W)PROTEIN?)

OR HSP?)/TI S38 14 S13 AND ((HEAT(W)SHOCK(W)PROTEIN?) OR HSP?)/TI S39 87 S10 AND ((FIBROBLAST(W)GROWTH(W)FACTOR?) OR FGF??) S40 5 S13 AND ((FIBROBLAST(W)GROWTH(W)FACTOR?) OR FGF??)/TI S41 25493 BLOOD(W)GROUP?
S42 14 S10 AND (BLOOD(W)GROUP?)/TI
S43 1 S10 AND (ABO)/TI
S44 115 S13 AND (RH OR RH(W)FACTORS?)
S45 33 S10 AND (RH OR RH(W)FACTORS?)/TI
?s (colloid?/ti and toxic?/ti)

3283 COLLOID?/TI
42730 TOXIC?/TI
S46 11 (COLLOID?/TI AND TOXIC?/TI)
?t s46/6/1-11

46/6/1
07803706 91322706
Toxic effects of ***colloids*** in the intensive care unit.

46/6/2
07790835 91309835
Four-week inhalation ***toxicity*** study with Ludox ***colloidal*** silica in rats: pulmonary cellular responses.

46/6/3
07519775 91038775
Preparation and evaluation of sterically stabilized liposomes: ***colloidal*** stability, serum stability, macrophage uptake, and ***toxicity***.

46/6/4
07051046 89353046
Reversible ***toxicity*** in poisoning with ***colloidal*** bismuth subcitrate.

46/6/5
06641362 88286362
Toxicity of solubilized and ***colloidal*** amphotericin B formulations to human erythrocytes.

46/6/6
06637458 88282458
Pharmacologic evaluation of ***toxicity*** after repeated administration of Duxon, a synthetic ***colloid*** solution]
Farmakologicke hodnoceni ***toxicity*** po opakovanem podavani syntetickeho koloidniho roztoku Duxonu.

46/6/7
06381926 88026926
Toxicity after repeated monthly administration of Duxon, a ***colloidal*** solution, to experimental rats]
Toxicita po opakovanem mesicnim podavani koloidniho roztoku Duxonu pokusnym krysam.

46/6/8
01825682 72075682
Intensification of the ***toxic*** effect of methotrexate following preliminary administration of ***colloidal*** gold to animals] Usilenie toksicheskogo deistviia metotreksata posle predvaritel'nogo vvedeniia zhivotnym kolloidnogo zolota.

46/6/9
01740061 71285061
Influence of ***colloidal*** ferrihexacyanoferrate (2) on distribution and ***toxicity*** of thallium] Der Einfluss von kolloidalem Ferrihexacyanoferrat (II) auf die Verteilung und ***Toxicitat*** von Thallium.

46/6/10
00381929 67206929
Animal ***toxicity*** studies of a ferric oxide ***colloid*** suitable for marrow scanning.

46/6/11
00262982 67087982
The ***toxicity*** and pyrogenicity of ***colloidal*** preparations of Au198 and CrP-32 O4 in neuro-oncological practice]
Toksichnost' i prirogennost' kolloidnykh Au198 i CrP-32 O-4 v neiroonkologicheskoi praktike.
?display sets